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(54) Title: SUCCINOYLAMINO CARBOCYCLES AND HETEROCYCLES AS INHIBITORS OF Aβ PROTEIN PRODUCTION

(57) Abstract: This invention relates to novel carbocycles and heterocycles having drug and bio-affecting properties, their pharmaceutical compositions and methods of use. These novel compounds inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurological deposits of amyloid protein. More particularly, the present invention relates to the treatment of neurological disorders related to β-amyloid production such as Alzheimer's disease and Down's Syndrome.

TITLE

SUCCINOYLAMINO CARBOCYCLES AND HETEROCYCLES AS INHIBITORS OF Aβ PROTEIN PRODUCTION

FIELD OF THE INVENTION

This invention relates to novel lactams having drug and bio-affecting properties, their pharmaceutical compositions and methods of use. These novel compounds inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurological deposits of amyloid protein. More particularly, the present invention relates to the treatment of neurological disorders related to β-amyloid production such as Alzheimer's disease and Down's Syndrome.

BACKGROUND OF THE INVENTION

Alzheimer's disease (AD) is a degenerative brain disorder characterized clinically by progressive loss of memory, temporal and local orientation, cognition, reasoning, judgment and emotional stability. AD is a common cause of progressive dementia in humans and is one of the major causes of death in the United States. AD has been observed in all races and ethnic groups worldwide, and is a major present and future health problem. No treatment that effectively prevents AD or reverses the clinical symptoms and underlying pathophysiology is currently available (for review, Dennis J. Selkoe; Cell Biology of the amyloid (beta)-protein precursor and the mechanism of Alzheimer's disease, Annu Rev Cell Biol, 1994, 10: 373-403).

Histopathological examination of brain tissue derived upon autopsy or from neurosurgical specimens in effected individuals revealed the occurrence of amyloid plaques and neurofibrillar tangles in the cerebral cortex of such patients. Similar alterations were observed in patients with Trisomy 21 (Down's syndrome), and hereditary cerebral hemorrhage with amyloidosis of the Dutch-type. Neurofibrillar tangles are nonmembrane-bound bundles of abnormal proteinaceous filaments and biochemical and immunochemical studies led to the conclusion that their principle protein subunit is an altered phosphorylated form of the tau protein (reviewed in Selkoe, 1994).

Biochemical and immunological studies revealed that the dominant proteinaceous component of the amyloid plaque is an approximately 4.2 kilodalton (kD) protein of about 39 to 43 amino acids. This protein was designated Aβ, β-amyloid peptide, and sometimes β/A4; referred to herein as Aβ. In addition to deposition of Aβ in amyloid plaques, Aβ is also found in the walls of meningeal and parenchymal arterioles, small arteries, capillaries, and sometimes, venules. Aβ was first purified, and a partial amino acid reported, in 1984 (Glenner and Wong, Biochem. Biophys. Res. Commun. 120: 885-890). The isolation and sequence data for the first 28 amino acids are described in U.S. Pat. No 4,666,829.

Compelling evidence accumulated during the last decade revealed that Aβ is an internal polypeptide derived from a type 1 integral membrane protein, termed b amyloid precursor protein (APP). β APP is normally produced by many cells both in vivo and in cultured cells, derived from various animals and humans. Aβ is derived from cleavage of β APP by as yet unknown enzyme (protease) system(s), collectively termed secretases.

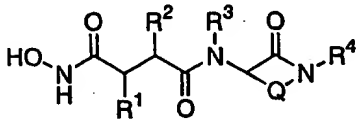
The existence of at least four proteolytic activities has been postulated. They include β secretase(s), generating the N-terminus of Aβ, a secretase(s) cleaving around the 16/17 peptide bond in Aβ, and γ secretases, generating C-terminal Aβ fragments ending at position 38, 39, 40, 42, and 43 or generating C-terminal extended precursors which are subsequently truncated to the above polypeptides.

Several lines of evidence suggest that abnormal accumulation of Aβ plays a key role in the pathogenesis of AD. Firstly, Aβ is the major protein found in amyloid plaques. Secondly, Aβ is neurotoxic and may be causally related to neuronal death observed in AD patients. Thirdly, missense DNA mutations at position 717 in the 770 isoform of β APP can be found in effected members but not unaffected members of several families with a genetically determined (familiar) form of AD. In addition, several other b APP mutations have been described in familiar forms of AD. Fourthly, similar neuropathological changes have been observed in transgenic animals overexpressing mutant forms of human β APP. Fifthly, individuals with Down's syndrome have an increased gene dosage of b APP and develop early-onset AD. Taken together, these observations strongly suggest that Aβ depositions may be causally related to the AD.

It is hypothesized that inhibiting the production of Aβ will prevent and reduce neurological degeneration, by controlling the formation of amyloid plaques, reducing neurotoxicity and, generally, mediating the pathology associated with Aβ production. One method of treatment methods would therefore be based on drugs that inhibit the formation of Aβ in vivo.

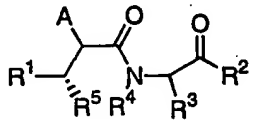
Methods of treatment could target the formation of Aβ through the enzymes involved in the proteolytic processing of β amyloid precursor protein. Compounds that inhibit β or γ secretase activity, either directly or indirectly, could control the production of Aβ. Advantageously, compounds that specifically target γ secretases, could control the production of Aβ. Such inhibition of β or γ secretases could thereby reduce production of Aβ, which, thereby, could reduce or prevent the neurological disorders associated with Aβ protein.

PCT publication number WO 96/29313 discloses the general formula:



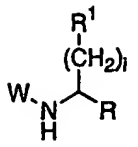
covering metalloprotease inhibiting compounds useful for the treatment of diseases associated with excess and/or unwanted matrix metalloprotease activity, particularly collagenase and or stromelysin activity.

Compounds of general formula:



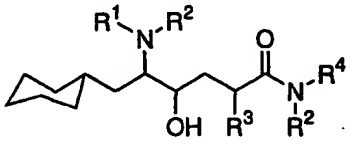
are disclosed in PCT publication number WO 95/22966 relating to matrix metalloprotease inhibitors. The compounds of the invention are useful for the treatment of conditions associated with the destruction of cartilage, including corneal ulceration, osteoporosis, periodontitis and cancer.

European Patent Application number EP 0652009A1 relates to the general formula:



and discloses compounds that are protease inhibitors that inhibit Aβ production.

US Patent Number 5703129 discloses the general formula:



which covers 5-amino-6-cyclohexyl-4-hydroxy-hexanamide derivatives that inhibit Aβ production and are useful in the treatment of Alzheimer's disease.

None of the above references teaches or suggests the compounds of the present invention which are described in detail below.

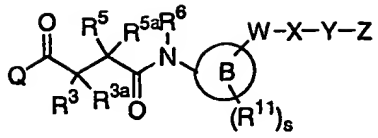
SUMMARY OF THE INVENTION

One object of the present invention is to provide novel compounds which are useful as inhibitors of the production of Aβ protein or pharmaceutically acceptable salts or prodrugs thereof.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide a method for treating degenerative neurological disorders comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

These and other objects, which will become apparent during the following detailed description, have been achieved by the inventors' discovery that compounds of Formula (I):

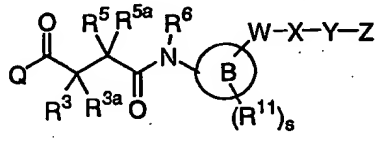


(I)

or pharmaceutically acceptable salt or prodrug forms thereof, wherein R^3, R^{3a}, R^5, R^{5a}, R^6, Q, B, W, X, Y, and Z are defined below, are effective inhibitors of the production of Aβ.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Thus, in a first embodiment, the present invention provides a novel compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

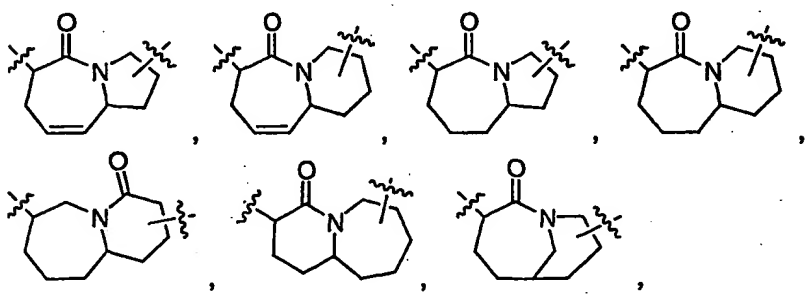
Q is $-OR^1$ or $-NR^1R^2$;

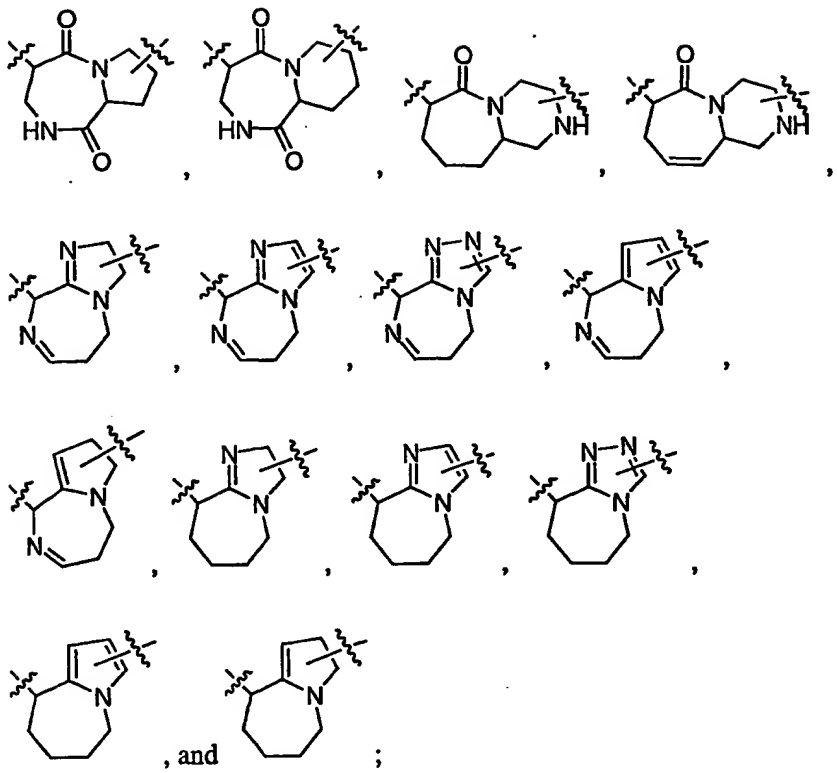
ring B is selected from the group consisting of:

a carbocyclic group of 3 to 8 carbon atoms wherein the carbocyclic group is saturated, partially saturated or unsaturated;

a heterocycle of 3 to 8 atoms containing a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, $-S(=O)_2-$, and $-N(R^{10})-$;

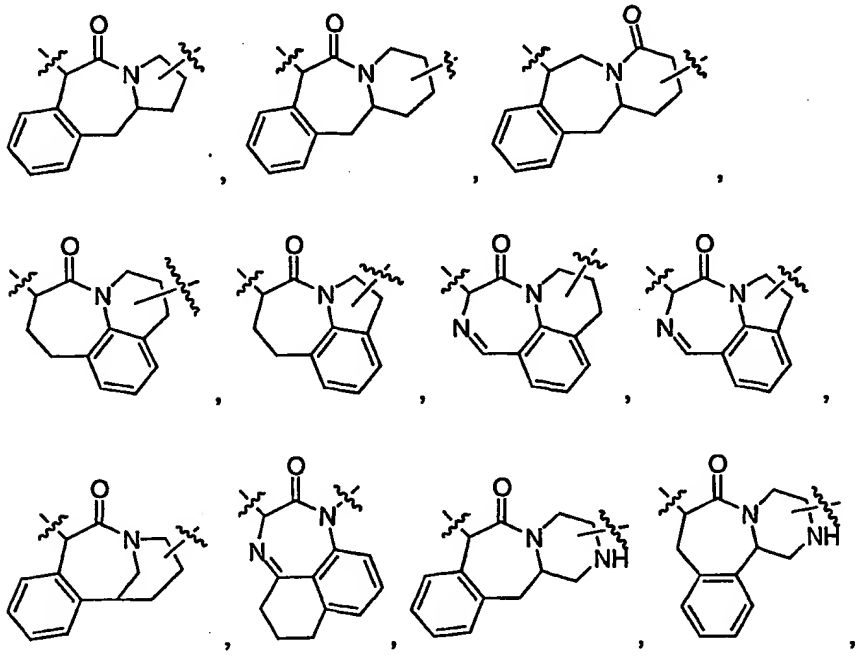
a bicyclic ring system selected from the group consisting of:

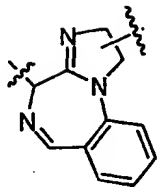




, and ;

a tricyclic ring system selected from the group consisting of:

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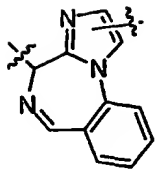
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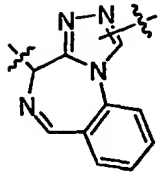
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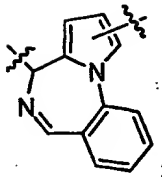
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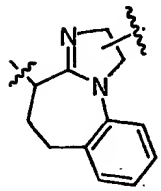
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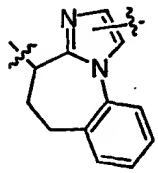
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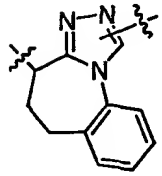
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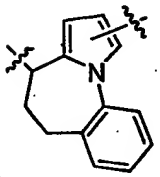
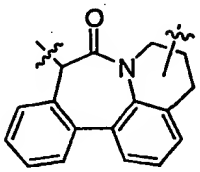

;

and

a tetracyclic ring system selected from the group consisting of: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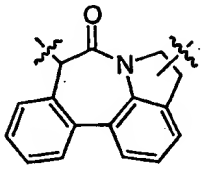


s is 0, 1, 2, 3, 4, 5, or 6;

R^1, at each occurrence, is independently selected from:

H;

C_1-C_6 alkyl substituted with 0-3 R^{1a};

C_2-C_6 alkenyl substituted with 0-3 R^{1a};

C_3-C_{10} carbocycle substituted with 0-3 R^{1b};

C_6-C_{10} aryl substituted with 0-3 R^{1b}; and

5 to 10 membered heterocycle substituted with 0-3 R^{1b};

R^{1a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3;

C_3-C_{10} carbocycle substituted with 0-3 R^{1b};

C_6-C_{10} aryl substituted with 0-3 R^{1b}; and

5 to 6 membered heterocycle substituted with 0-3 R^{1b};

R^{1b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^2 is independently selected from H, NH_2, OH, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenoxy, benzyloxy, C_3-C_{10} carbocycle, C_6-C_{10} aryl and 5 to 10 membered heterocycle;

R^3 is $-(CR^7R^{7a})_n-R^4$,
$-(CR^7R^{7a})_n-S-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-O-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-S(=O)-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-S(=O)_2-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-C(=O)-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})C(=O)-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-C(=O)N(R^{7b})-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})S(=O)_2-(CR^7R^{7a})_m-R^4$, or
$-(CR^7R^{7a})_n-S(=O)_2N(R^{7b})-(CR^7R^{7a})_m-R^4$;

n is 0, 1, 2, or 3;

m is 0, 1, 2, or 3;

R^{3a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, or C_2-C_4 alkenyloxy;

alternatively, R^3 and R^{3a} may be combined to form a 3-7 membered carbocyclic moiety;
wherein said 3-7 membered carbocyclic moiety is saturated or partially unsaturated;
wherein said 3-7 membered carbocyclic moiety may optionally contain a heteroatom selected from -O-, -S-, -S(=O)-, $-S(=O)_2-$, -N=, -NH-, and $-N(R^{20})-$, and
wherein said 3-7 membered carbocyclic moiety is substituted with 0-4 R^4;

additionally, two R^4 substituents on adjacent atoms may be combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{23};

additionally, two R^4 substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl

fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R^{23};

additionally, two R^4 substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle substituted with 0-3 R^{23};

R^4 is H, OH, OR^{14a},
C_1-C_6 alkyl substituted with 0-3 R^{4a},
C_2-C_6 alkenyl substituted with 0-3 R^{4a},
C_2-C_6 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, Br, I, CF_3,
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^5 is H, OR^{14};
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_1-C_6 alkoxy substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3R^{5c};

R^{5a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_2-C_4 alkenyl, or C_2-C_4 alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^5 and R^{5a} may be combined to form a 3-7 membered carbocyclic ring substituted with 0-3 R^{5c}; optionally the carbocyclic ring formed by combining R^5 and R^{5a} may be benzo fused, wherein the benzo fused ring may be substituted with 0-3 R^{5c};

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^7, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, and C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, aryl and C_1-C_4 alkyl;

R^{7b} is independently selected from H and C_1-C_4 alkyl;

W is $-(CR^8R^{8a})_p-$;

p is 0, 1, 2, 3, or 4;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

Y is a bond or $-(CR^9R^{9a})_t$-V-$(CR^9R^{9a})_u$-;

t is 0, 1, 2, or 3;

u is 0, 1, 2, or 3;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, $-S(=O)_2$-, $-N(R^{19})$-, $-C(=O)NR^{19b}$-, $-NR^{19b}C(=O)$-, $-NR^{19b}S(=O)_2$-, $-S(=O)_2NR^{19b}$-, $-NR^{19b}S(=O)$-, $-S(=O)NR^{19b}$-, -C(=O)O-, or -OC(=O)-;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a};
C_2-C_4 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12a};
C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_1-C_3 alkyl substituted with 0-1 R^{12c};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{12c}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl substituted with 0-2 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^{10} may be -W-X-Y-Z;

R^{11}, at each occurrence, is independently selected from
H, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl substituted with 0-1 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{13};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14}, at each occurrence, is independently selected from H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{17} is H, aryl, aryl-CH_2-, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring;

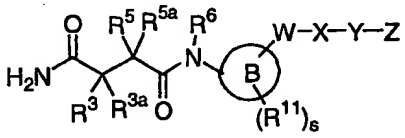
R^{20} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$; C_1-C_6 alkyl optionally substituted with 0-3 R^{20a}; or C_6-C_{10} aryl substituted with 0-4 R^{20b};

R^{20a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{20b};

R^{20b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{23}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3.

[2] In a preferred embodiment the present invention provides a compound of Formula (Ia):



(Ia)

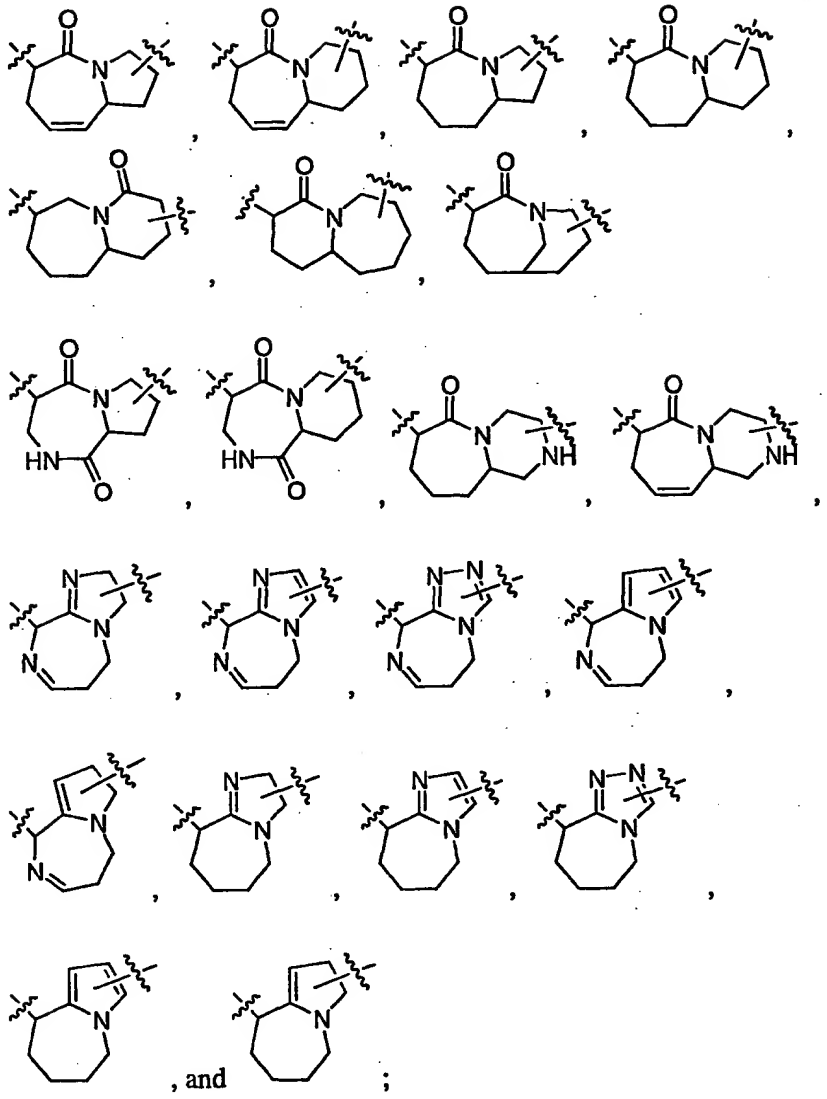
or a pharmaceutically acceptable salt or prodrug thereof, wherein:

ring B is selected from the group consisting of:

a carbocyclic group of 5 to 7 carbon atoms wherein the carbocyclic group is saturated, partially saturated or unsaturated;

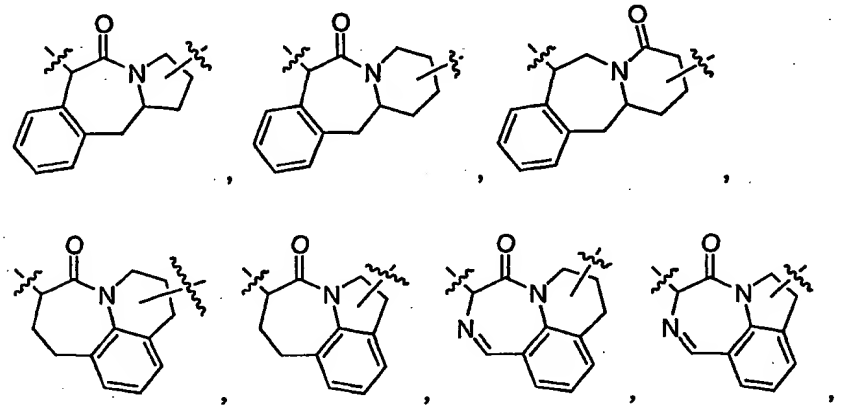
a heterocycle of 5 to 7 atoms containing a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, $-S(=O)_2-$, and $-N(R^{10})-$;

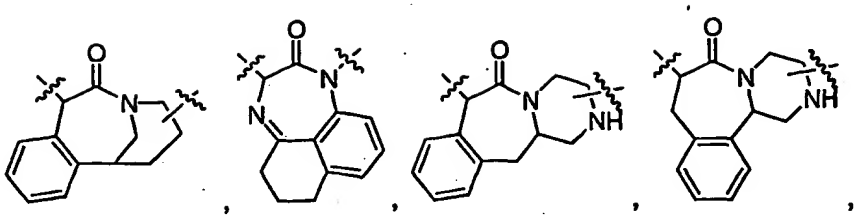
a bicyclic ring system selected from the group consisting of:



, and ;

a tricyclic ring system selected from the group consisting of:

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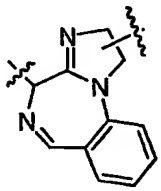
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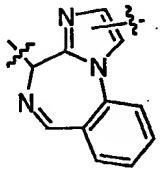
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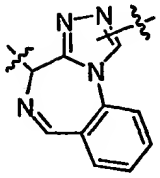
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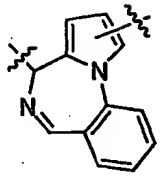
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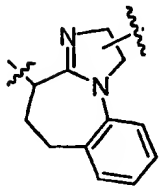
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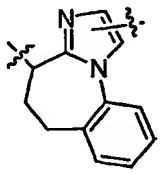
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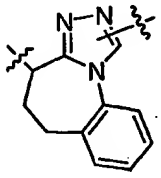
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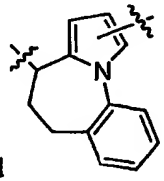
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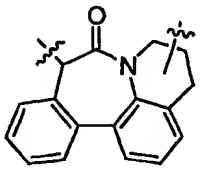
and

a tetracyclic ring system selected from the group consisting of: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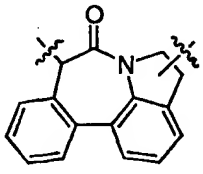


s is 0, 1, 2, 3, or 4;

R^3 is $-(CR^7R^{7a})_n-R^4$,
$-(CR^7R^{7a})_n-S-R^4$,
$-(CR^7R^{7a})_n-O-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})-R^4$,
$-(CR^7R^{7a})_n-S(=O)-R^4$,
$-(CR^7R^{7a})_n-S(=O)_2-R^4$, or
$-(CR^7R^{7a})_n-C(=O)-R^4$;

n is 0, 1, or 2;

R^{3a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, or C_2-C_4 alkenyloxy;

alternatively, R^3 and R^{3a} may be combined to form a 3-7 membered carbocyclic moiety;
wherein said 3-7 membered carbocyclic moiety is saturated or partially unsaturated;
wherein said 3-7 membered carbocyclic moiety may optionally contain a heteroatom selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, -N=, -NH-, and -N(R^{20})-, and
wherein said 3-7 membered carbocyclic moiety is substituted with 0-4 R^4;

additionally, two R^4 substituents on adjacent atoms may be combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{23};

additionally, two R^4 substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R^{23};

additionally, two R^4 substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle substituted with 0-3 R^{23};

R^4 is H, OH, OR^{14a},
C_1-C_6 alkyl substituted with 0-3 R^{4a},
C_2-C_6 alkenyl substituted with 0-3 R^{4a},
C_2-C_6 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, Br, I, CF_3,
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c}; or
C_6-C_{10} aryl substituted with 0-3 R^{5c};

R^{5a} is H, C_1-C_4 alkyl, or C_2-C_4 alkenyl;

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^5 and R^{5a} may be combined to form a 3-7 membered carbocyclic ring substituted with 0-3 R^{5c}; optionally the carbocyclic ring formed by combining R^5 and R^{5a} may be benzo fused, wherein the benzo fused ring may be substituted with 0-3 R^{5c};

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^7, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, and C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, aryl and C_1-C_4 alkyl;

R^{7b} is independently selected from H and C_1-C_4 alkyl;

W is $-(CR^8R^{8a})_p-$;

p is 0, 1, 2, or 3;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

Y is a bond or $-(CR^9R^{9a})_t-V-(CR^9R^{9a})_u-$;

t is 0, 1, 2, or 3;

u is 0, 1, 2, or 3;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, -C(=O)O-, or -OC(=O)-;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a};

C_2-C_4 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12a};
C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12a}; or

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, -C(=O)$NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_1-C_3 alkyl substituted with 0-1 R^{12c};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^{12c}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{10} is H, C(=O)R^{17}, C(=O)OR^{17}, C(=O)$NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl substituted with 0-2 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^{10} may be -W-X-Y-Z;

R^{11}, at each occurrence, is independently selected from H,
C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl substituted with 0-1 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{13};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14}, at each occurrence, is independently selected from H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{17} is H, aryl, aryl-CH_2-, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring;

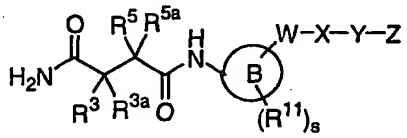
R^{20} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl optionally substituted with 0-3 R^{20a}; or
C_6-C_{10} aryl substituted with 0-4 R^{20b};

R^{20a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{20b};

R^{20b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{23}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3.

[3] In another preferred embodiment the present invention provides a compound of Formula (Ia):



(Ia)

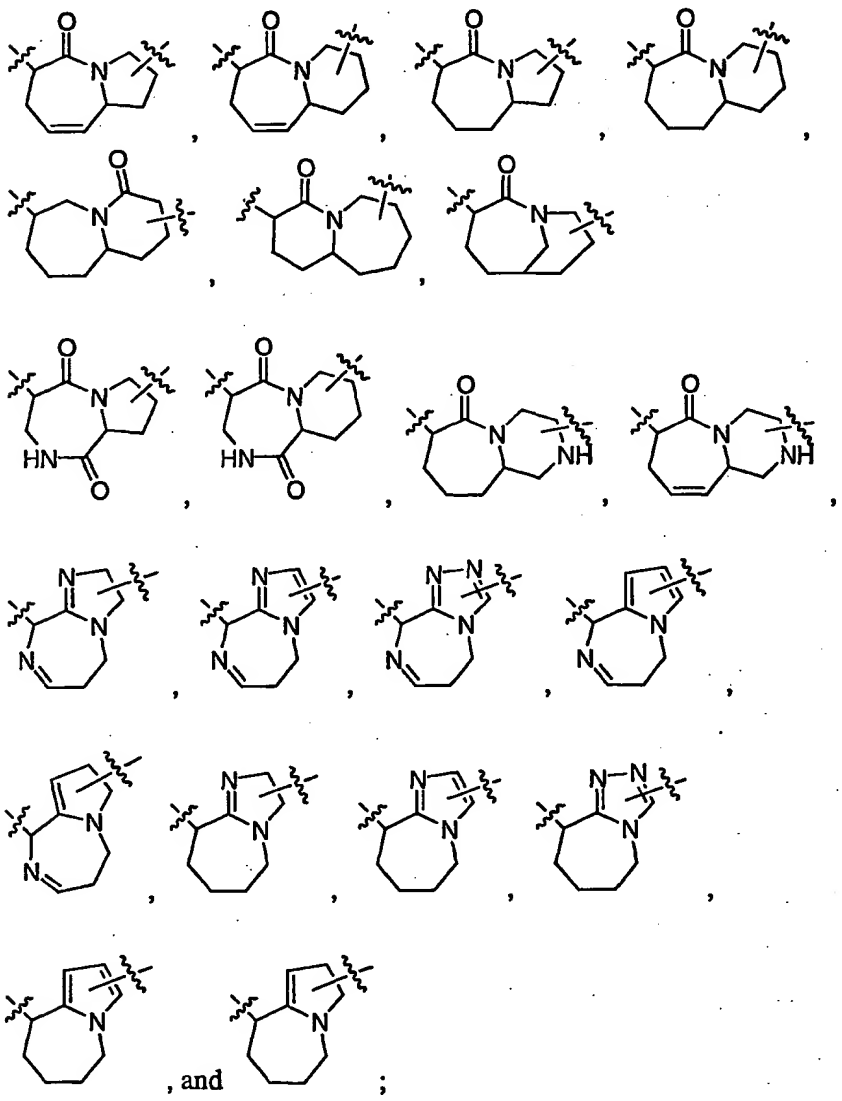
or a pharmaceutically acceptable salt or prodrug thereof, wherein:

ring B is selected from the group consisting of:

a carbocyclic group of 5, 6, or 7 carbon atoms selected from -cyclopentylene-, -cyclohexylene-, -cycloheptylene-, -cyclopentenylene-, -cyclohexenylene-, and -phenylene-;

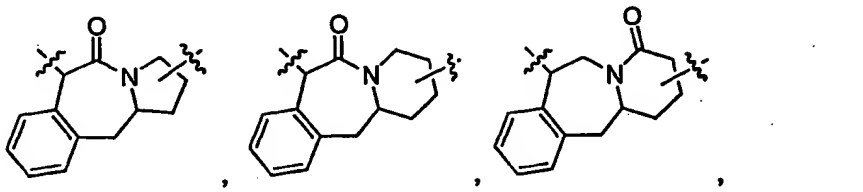
a heterocycle of 5, 6, or 7 atoms selected from -pyrrolidinylene-, -piperidinylene-, -homopiperidinylene-, and -thiophenylene-;

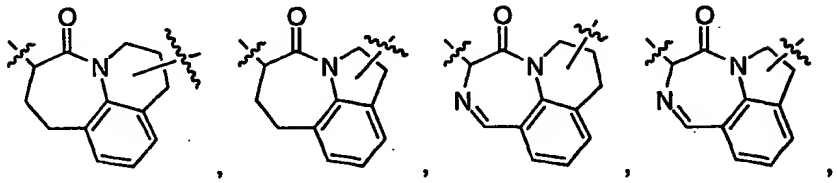
a bicyclic ring system selected from the group consisting of:

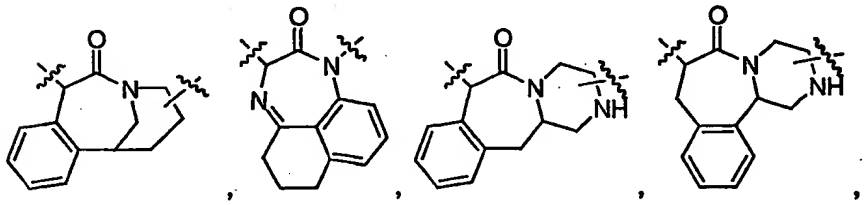


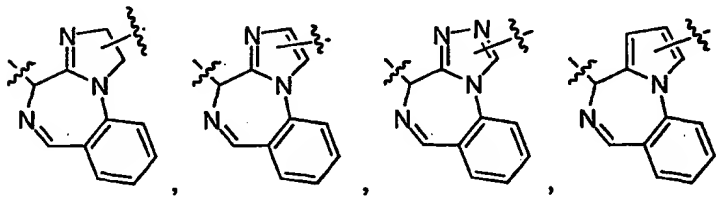
, and ;

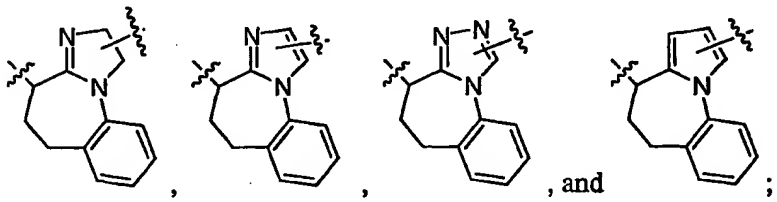
a tricyclic ring system selected from the group consisting of:





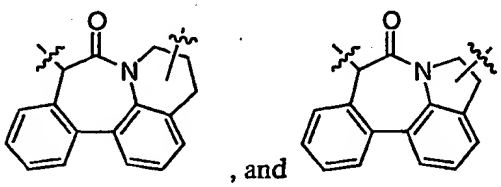






and

a tetracyclic ring system selected from the group consisting of:



s is 0, 1, 2, 3, or 4;

R^3 is $-(CH_2)_n-R^4$;

n is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, or butoxy;

alternatively, R^3 and R^{3a} may be combined to form a 3-7 membered carbocyclic moiety;
wherein said 3-7 membered carbocyclic moiety is saturated or partially unsaturated;
wherein said 3-7 membered carbocyclic moiety is substituted with 0-2 R^4;

R^4 is H, OH,
C_1-C_4 alkyl substituted with 0-2 R^{4a},
C_2-C_4 alkenyl substituted with 0-2 R^{4a},
C_2-C_4 alkynyl substituted with 0-1 R^{4a},
C_3-C_6 cycloklyl substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, CF_3,
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^5 is H;
C_1-C_4 alkyl substituted with 0-2 R^{5b};
C_2-C_4 alkenyl substituted with 0-2 R^{5b};
C_2-C_4 alkynyl substituted with 0-2 R^{5b};
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c}; or
phenyl substituted with 0-3 R^{5c};

R^{5a} is H, methyl, ethyl, propyl, butyl, or allyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, OR^{14},
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle substituted with 0-2 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

alternatively, R^5 and R^{5a} may be combined to form a 3-7 membered carbocyclic ring substituted with 0-3 R^{5c};

W is a bond, $-CH_2-$, $-CH(CH_3)-$, $-CH_2CH_2-$ or $-CH(CH_3)CH_2-$;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-2 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Y is a bond, $-CH_2CH_2-V-$, $-CH_2-V-$, or $-V-$;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a};
C_2-C_4 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12a};
C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12a}; or

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_1-C_3 alkyl substituted with 0-1 R^{12c};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{12c}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{11}, at each occurrence, is independently selected from H,
C_1-C_4 alkoxy, Cl, F, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF_3;
C_1-C_4 alkyl substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{17} is H, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-methylphenyl, 4-trifluorophenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-methylphenyl)methyl, (4-trifluorophenyl)methyl, methyl, ethyl, propyl, butyl, methoxymethyl, methyoxyethyl, ethoxymethyl, or ethoxyethyl;

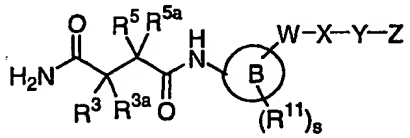
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl;

R^{19b} is H, mehyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring.

[4] In another preferred embodiment the present invention provides a compound of Formula (Ia):

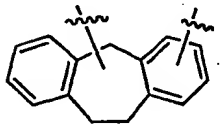


(Ia)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

ring B is selected from the group consisting of:

-cyclopent-1,2-diyl-, -cyclopent-1,3-diyl-, -cyclohex-1,2-diyl-, -cyclohex-1,3-diyl-, -cyclohex-1,4-diyl-, -cyclohept-1,3-diyl-, -cyclopenten-3,5-diyl-, -phen-1,2-diyl-, -phen-1,3-diyl-, -phen-1,4-diyl-, -pyrrolidin-1,4-diyl-, -pyrrolidin-2,4-diyl-, -piperidin-1,4-diyl-, -piperidin-1,3-diyl-, -thiophen-2,3-diyl-, and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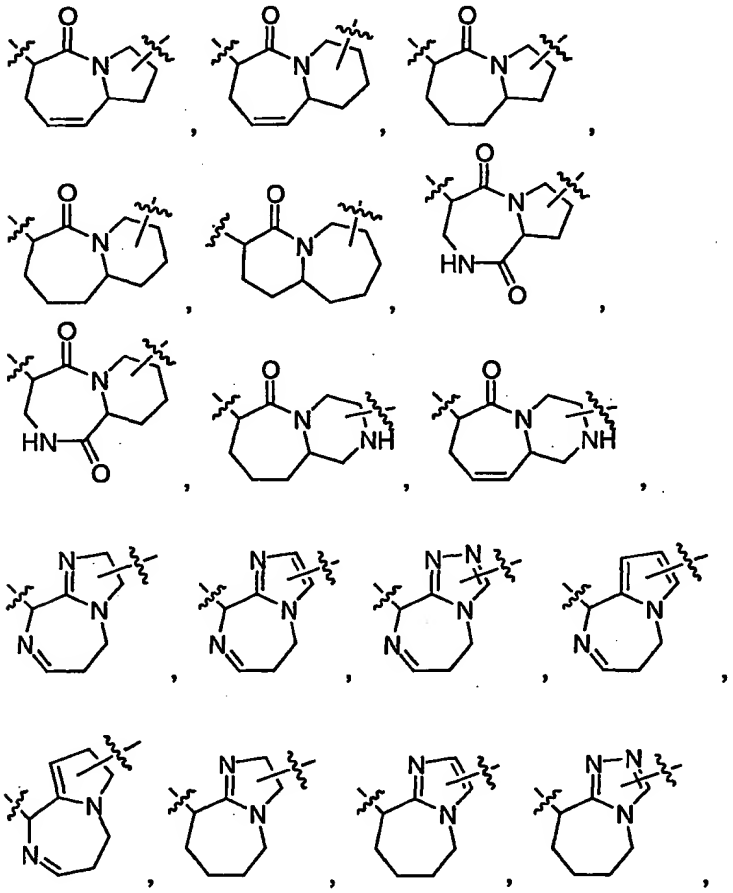
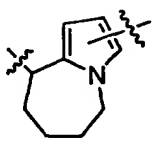
a bicyclic ring system selected from the group consisting of:

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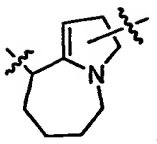
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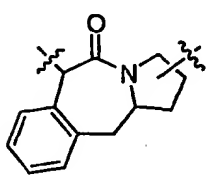
a tricyclic ring system selected from the group consisting of: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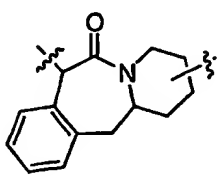
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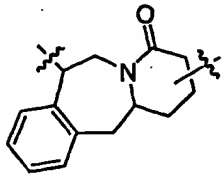
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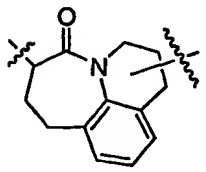
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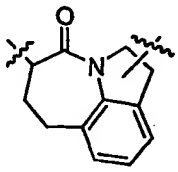
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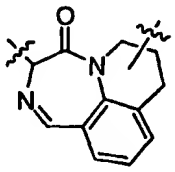
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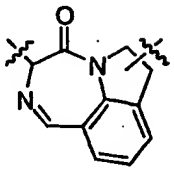
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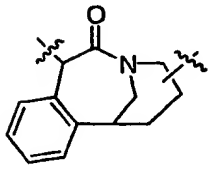
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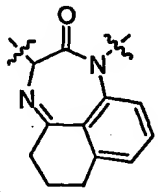
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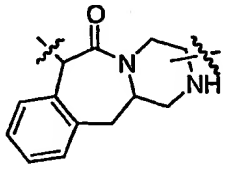
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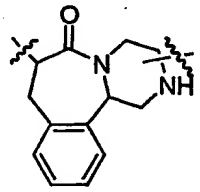
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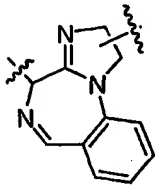
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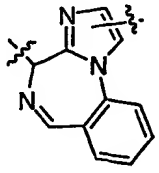
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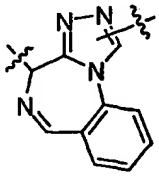
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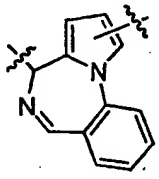
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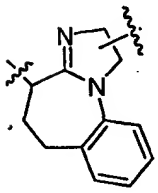
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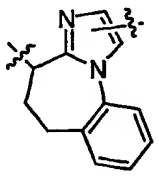
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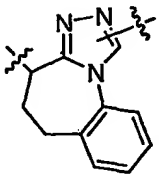
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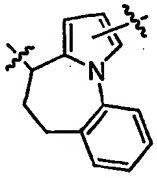
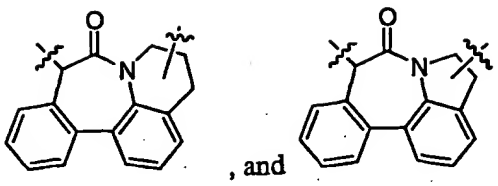

;

and

a tetracyclic ring system selected from the group consisting of:



s is 0, 1, or 2;

R^3 is $-R^4$, $-CH_2-R^4$, or $-CH_2CH_2-R^4$;

R^{3a} is H;

alternatively, R^3 and R^{3a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl moiety;

R^4 is H, C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_2-C_4 alkynyl;

R^5 is C_1-C_4 alkyl substituted with 0-1 R^{5b};
C_2-C_4 alkenyl substituted with 0-1 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-1 R^{5b};

R^{5a} is H;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, OR^{14},
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle substituted with 0-2 R^{5c};

alternatively, R^5 and R^{5a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl ring;

W is a bond, $-CH_2-$, $-CH(CH_3)-$, $-CH_2CH_2-$ or $-CH(CH_3)CH_2-$;

X is a bond, phenyl, pyridyl, cyclopentyl, cyclohexyl, piperidinyl, or pyrrolidinyl;

Y is a bond, $-CH_2CH_2-V-$, $-CH_2-V-$, or $-V-$;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$,

$-NR^{19b}C(=O)-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;

C_1-C_8 alkyl substituted with 0-3 R^{12a};

C_2-C_4 alkenyl substituted with 0-3 R^{12a};

C_2-C_4 alkynyl substituted with 0-3 R^{12a};

C_6-C_{10} aryl substituted with 0-2 R^{12a};

C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12a}; or

R^{12a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,

C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,

C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,

C_1-C_3 alkyl substituted with 0-1 R^{12c};

C_6-C_{10} aryl substituted with 0-4 R^{12b};

C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{12c}, at each occurrence, is independently selected from

C_6-C_{10} aryl substituted with 0-4 R^{12b};

C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{11}, at each occurrence, is independently selected from

H, C_1-C_4 alkoxy, Cl, F, =O, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF_3;

C_1-C_4 alkyl substituted with 0-1 R^{11a};

phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{17} is H, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-methylphenyl, 4-trifluorophenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-methylphenyl)methyl, (4-trifluorophenyl)methyl, methyl, ethyl, propyl, butyl, methoxymethyl, methyoxyethyl, ethoxymethyl, or ethoxyethyl;

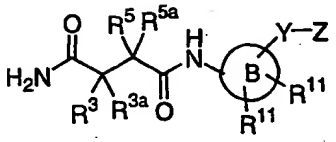
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl;

R^{19b} is H, mehyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring.

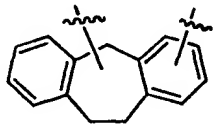
[5] In another preferred embodiment the present invention provides a compound of Formula (Ic):

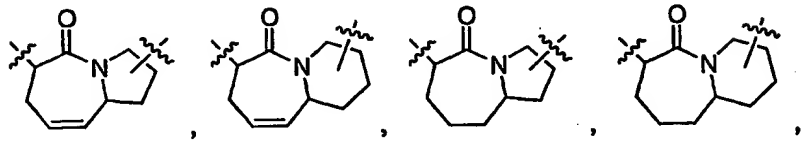


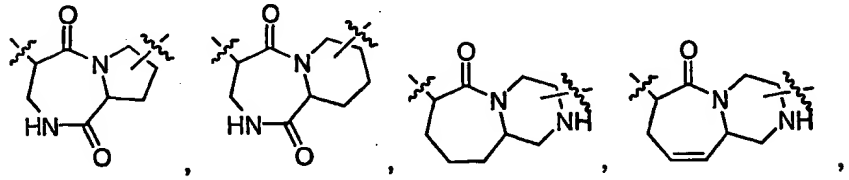
(Ic)

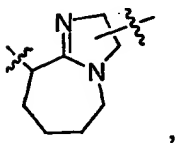
or a pharmaceutically acceptable salt or prodrug thereof, wherein:

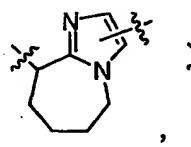
ring B is selected from the group consisting of:

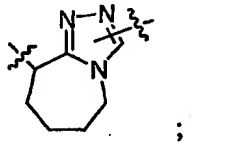
 ,

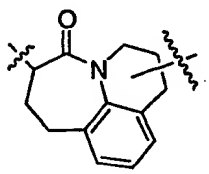
 ,

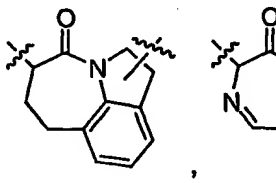
 ,

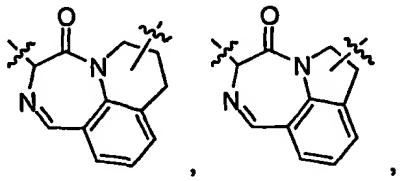
 ,

 ,

 ;

 ,

 ,

 ,

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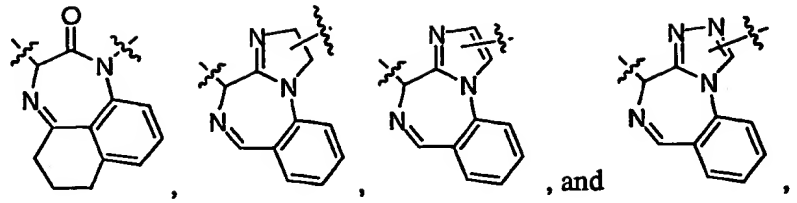


R^3 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_3$, $-CH_2(CH_3)_2$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, $-CH=CH_2$, $-CH_2CH=CH_2$, $-CH_2C(CH_3)=CH_2$, $-CH_2CH=C(CH_3)_2$, $-CH_2CH_2CH=CH_2$, $-CH_2CH_2C(CH_3)=CH_2$, $-CH_2CH_2CH=C(CH_3)_2$, cis-$CH_2CH=CH(CH_3)$, cis-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(CH_3)$, trans-$CH_2CH_2CH=CH(CH_3)$, $-C\equiv CH$, $-CH_2C\equiv CH$, or $-CH_2C\equiv C(CH_3)$;

R^{3a} is H;

alternatively, R^3 and R^{3a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl moiety;

R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_2CH_3$, $-CH_2CH(CH_3)CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH(CH_2CH_3)_2$, $-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$, cis-$CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(CH_3)$, $-CH_2CH=C(CH_3)_2$, cis-$CH_2CH=CHCH_2CH_3$, trans-$CH_2CH=CHCH_2CH_3$, cis-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH_2CH=CH(CH_3)$, $-C\equiv CH$, $-CH_2C\equiv CH$, $-CH_2C\equiv C(CH_3)$, $-CH_2CH_2C\equiv CH$, or $-CH_2CH_2C\equiv C(CH_3)$;

R^{5a} is H;

alternatively, R^5 and R^{5a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl ring;

Y is a bond, $-CH_2CH_2$-V-, $-CH_2$-V-, or -V-;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, -S(=O)$_2$-, -N(R^{19})-, -C(=O)NR^{19b}-, -NR^{19b}C(=O)-, -C(=O)O-, or -OC(=O)-;

Z is H;

C_1-C_4 alkyl substituted with 0-1 R^{12a};

C_2-C_4 alkenyl substituted with 0-1 R^{12a};

C_2-C_4 alkynyl substituted with 0-1 R^{12a};

phenyl substituted with 0-2 R^{12a};

C_3-C_6 cycloalkyl, selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; substituted with 0-2 R^{12a}; or

5 to 10 membered heterocycle selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrrolidinyl, piperidinyl, N-piperinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, morpholinyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl; wherein said 5 to 10 membered heterocycle is substituted with 0-2 R^{12a};

R^{12a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, CN, NO_2, N$R^{15}R^{16}$, -C(=O)N$R^{15}R^{16}$, CF_3, acetyl, SCH_3, SCF_3, S(=O)CH_3, S(=O)$_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, C_1-C_2 haloalkyl, C_1-C_2 haloalkoxy,

C_1-C_3 alkyl substituted with R^{12c};

phenyl substituted with 0-3 R^{12b};

5 to 10 membered heterocycle selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrrolidinyl, piperidinyl, N-piperinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, morpholinyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl; wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, N$R^{15}R^{16}$, CF_3, acetyl, SCH_3, S(=O)CH_3, S(=O)$_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{12c}, at each occurrence, is independently selected from

phenyl substituted with 0-4 R^{12b};
C_3-C_{10} cycloalkyl, selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrrolidinyl, piperidinyl, N-piperinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, morpholinyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl; wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{11}, at each occurrence, is independently selected from H, Cl, F, $NR^{18}R^{19}$, methyl, ethyl, methoxy, ethoxy, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, or (4-CF_3-phenyl)CH_2CH_2-; and

R^{15}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, propyl-C(=O)-, butyl-C(=O)-, methyl-$S(=O)_2$-, ethyl- $S(=O)_2$-, propyl-$S(=O)_2$-, and butyl-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, propyl-C(=O)-, butyl-C(=O)-, methyl-$S(=O)_2$-, ethyl- $S(=O)_2$-, propyl-$S(=O)_2$-, and butyl-$S(=O)_2$-;

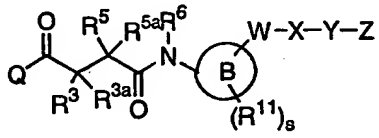
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl;

R^{19b} is H, mehyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, and morpholinyl.

[6] In another embodiment the present invention provides a compound of Formula (I):

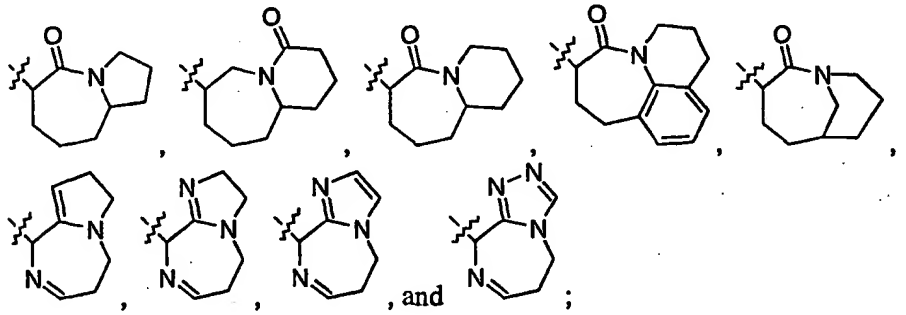


(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is NH_2;

ring B is cycloalkyl group of 3 to 8 carbon atoms wherein the cycloalkyl group is saturated, partially saturated or unsaturated; a heterocycle of 3 to 8 atoms containing a heteroatom selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, and -N(R^{10})-;



, and ;

s is 0, 1, 2, 3, 4, 5, or 6;

R^3 is -$(CR^7R^{7a})_n$-R^4,
-$(CR^7R^{7a})_n$-S-$(CR^7R^{7a})_m$-R^4,
-$(CR^7R^{7a})_n$-O-$(CR^7R^{7a})_m$-R^4, or
-$(CR^7R^{7a})_n$-N(R^{7b})-$(CR^7R^{7a})_m$-R^4;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, or butoxy;

R^4 is H, OH, OR^{14a},
C_1-C_4 alkyl substituted with 0-2 R^{4a},
C_2-C_4 alkenyl substituted with 0-2 R^{4a},
C_2-C_4 alkynyl substituted with 0-2 R^{4a},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, Br, I CF_3,
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^5 is H, OR^{14};
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3R^{5c};

R^{5a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_2-C_4 alkenyl, or C_2-C_4 alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^6 is H, methyl, or ethyl;

R^7, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, and C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, phenyl and C_1-C_4 alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

W is $-(CR^8R^{8a})_p-$;

p is 0, 1, or 2;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl and C_3-C_6 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-2 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

Y is a bond or $-(CR^9R^{9a})_t$-V-$(CR^9R^{9a})_u-$;

t is 0, 1, or 2;

u is 0, 1, or 2;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl or C_3-C_6 cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, -S(=O)$_2$-, -N(R^{19})-, -C(=O)NR^{19b}-, -NR^{19b}C(=O)-, -NR^{19b}S(=O)$_2$-, -S(=O)$_2$NR^{19b}-, -NR^{19b}S(=O)-, or -S(=O)NR^{19b}-;

Z is C_1-C_3 alkyl substituted with 1-2 R^{12};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12} is C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, S(=O)CH_3, S(=O)$_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^{10} is H, C(=O)R^{17}, C(=O)OR^{17}, C(=O)N$R^{18}R^{19}$, S(=O)$_2$N$R^{18}R^{19}$, S(=O)$_2R^{17}$;
C_1-C_6 alkyl substituted with 0-1 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{11}, at each occurrence, is independently selected from
C_1-C_4 alkoxy, Cl, F, $NR^{18}R^{19}$, C(=O)R^{17}, C(=O)OR^{17}, C(=O)N$R^{18}R^{19}$, S(=O)$_2$N$R^{18}R^{19}$, CF_3;
C_1-C_6 alkyl substituted with 0-1 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{17} is H, aryl, (aryl)CH_2-, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl.

[7] In another preferred embodiment the present invention provides a compound of Formula (Ia) wherein:

R^3 is -$(CR^7R^{7a})_n$-R^4,
-$(CR^7R^{7a})_n$-S-$(CR^7R^{7a})_m$-R^4,
-$(CR^7R^{7a})_n$-O-$(CR^7R^{7a})_m$-R^4, or
-$(CR^7R^{7a})_n$-$N(R^{7b})$-$(CR^7R^{7a})_m$-R^4;

n is 0 or 1;

m is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, or butoxy;

R^4 is H, OH,
C_1-C_4 alkyl substituted with 0-2 R^{4a},
C_2-C_4 alkenyl substituted with 0-2 R^{4a},
C_2-C_4 alkynyl substituted with 0-1 R^{4a},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, CF_3,
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^5 is H, OR^{14};
C_1-C_4 alkyl substituted with 0-3 R^{5b};
C_2-C_4 alkenyl substituted with 0-2 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-2 R^{5b};

R^{5a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, or allyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, OR^{14}, =O;
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle substituted with 0-2 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^6 is H;

R^7, at each occurrence, is independently selected from H, F, CF_3, methyl, and ethyl;

R^{7a}, at each occurrence, is independently selected from H, F, CF_3, methyl, and ethyl;

R^{7b} is independently selected from H, methyl, and ethyl;

W is a bond, $-CH_2-$, $-CH(CH_3)-$, $-CH_2CH_2-$ or $-CH(CH_3)CH_2-$;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-2 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Y is a bond, $-CH_2-V-$, $-V-$, or $-V-CH_2-$;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, or $-N(CH_2CH_3)-$,

Z is C_1-C_2 alkyl substituted with 1-2 R^{12};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_6 carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12} is C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_6 carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$;
C_1-C_4 alkyl substituted with 0-1 R^{10a};

phenyl substituted with 0-4 R^{10b};
C_3-C_6 carbocycle substituted with 0-3 R^{10b}; or
5 to 6 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, C_1-C_3 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{11}, at each occurrence, is independently selected from
C_1-C_4 alkoxy, Cl, F, =O, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF_3;
C_1-C_4 alkyl substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -$S(=O)_2$-(C_1-C_4 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -$S(=O)_2$-(C_1-C_4 alkyl);

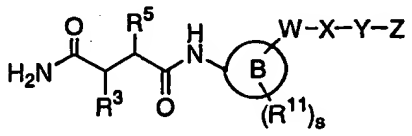
R^{17} is H, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-methylphenyl, 4-trifluorophenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-methylphenyl)methyl, (4-

trifluorophenyl)methyl, methyl, ethyl, propyl, butyl, methoxymethyl, methyoxyethyl, ethoxymethyl, or ethoxyethyl;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl.

[8] In another preferred embodiment the present invention provides a compound of Formula (Ib):



(Ib)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

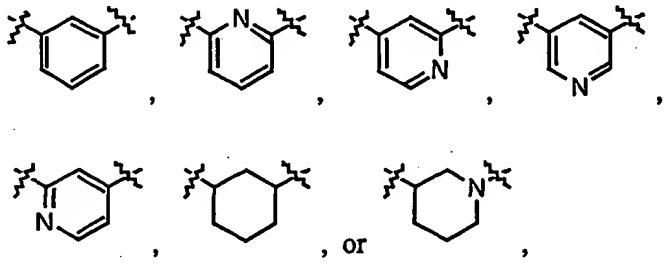
R^3 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_3$, $-CH_2(CH_3)_2$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, $-CF_3$, $-CH_2CF_3$, $-CH_2CH_2CF_3$, $-CH_2CH_2CH_2CF_3$, $-CH=CH_2$, $-CH_2CH=CH_2$, $-CH_2C(CH_3)=CH_2$, $-CH_2CH=C(CH_3)_2$, $-CH_2CH_2CH=CH_2$, $-CH_2CH_2C(CH_3)=CH_2$, $-CH_2CH_2CH=C(CH_3)_2$, cis-$CH_2CH=CH(CH_3)$, cis-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(CH_3)$, trans-$CH_2CH_2CH=CH(CH_3)$; $-C\equiv CH$, $-CH_2C\equiv CH$, $-CH_2C\equiv C(CH_3)$, cyclopropyl-CH_2-, cyclobutyl-CH_2-, cyclopentyl-CH_2-, cyclohexyl-CH_2-, cyclopropyl-CH_2CH_2-, cyclobutyl-CH_2CH_2-, cyclopentyl-CH_2CH_2-, cyclohexyl-CH_2CH_2-, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-, (3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, phenyl-CH_2CH_2-, (2-F-phenyl)CH_2CH_2-, (3-F-phenyl)CH_2CH_2-, (4-F-phenyl)CH_2CH_2-, (2-Cl-phenyl)CH_2CH_2-, (3-Cl-phenyl)CH_2CH_2-, (4-Cl-phenyl)CH_2CH_2-, (2,3-diF-phenyl)CH_2CH_2-, (2,4-diF-phenyl)CH_2CH_2-, (2,5-diF-phenyl)CH_2CH_2-, (2,6-diF-phenyl)CH_2CH_2-, (3,4-diF-phenyl)CH_2CH_2-, (3,5-diF-phenyl)CH_2CH_2-, (2,3-diCl-phenyl)CH_2CH_2-, (2,4-diCl-phenyl)CH_2CH_2-,

(2,5-diCl-phenyl)CH_2CH_2-, (2,6-diCl-phenyl)CH_2CH_2-,
(3,4-diCl-phenyl)CH_2CH_2-, (3,5-diCl-phenyl)CH_2CH_2-,
(3-F-4-Cl-phenyl)CH_2CH_2-, or (3-F-5-Cl-phenyl)CH_2CH_2-;

R^5 is -CH_3, -CH_2CH_3, -$CH_2CH_2CH_3$, -$CH_2(CH_3)_2$, -$CH_2CH_2CH_2CH_3$,
-$CH(CH_3)CH_2CH_3$, -$CH_2CH(CH_3)_2$, -$CH_2C(CH_3)_3$, -$CH_2CH_2CH_2CH_2CH_3$,
-$CH(CH_3)CH_2CH_2CH_3$, -$CH_2CH(CH_3)CH_2CH_3$, -$CH_2CH_2CH(CH_3)_2$,
-$CH(CH_2CH_3)_2$, -CF_3, -CH_2CF_3, -$CH_2CH_2CF_3$, -$CH_2CH_2CH_2CF_3$,
-$CH_2CH_2CH_2CH_2CF_3$, -$CH{=}CH_2$, -$CH_2CH{=}CH_2$, -$CH{=}CHCH_3$, cis-
$CH_2CH{=}CH(CH_3)$, trans-$CH_2CH{=}CH(CH_3)$, trans-$CH_2CH{=}CH(C_6H_5)$,
-$CH_2CH{=}C(CH_3)_2$, cis-$CH_2CH{=}CHCH_2CH_3$, trans-$CH_2CH{=}CHCH_2CH_3$,
cis-$CH_2CH_2CH{=}CH(CH_3)$, trans-$CH_2CH_2CH{=}CH(CH_3)$,
trans-$CH_2CH{=}CHCH_2(C_6H_5)$,
-$C{\equiv}CH$, -$CH_2C{\equiv}CH$, -$CH_2C{\equiv}C(CH_3)$, -$CH_2C{\equiv}C(C_6H_5)$,
-$CH_2CH_2C{\equiv}CH$, -$CH_2CH_2C{\equiv}C(CH_3)$, -$CH_2CH_2C{\equiv}C(C_6H_5)$,
-$CH_2CH_2CH_2C{\equiv}CH$, -$CH_2CH_2CH_2C{\equiv}C(CH_3)$, -$CH_2CH_2CH_2C{\equiv}C(C_6H_5)$,
cyclopropyl-CH_2-, cyclobutyl-CH_2-, cyclopentyl-CH_2-, cyclohexyl-CH_2-,
(2-CH_3-cyclopropyl)CH_2-, (3-CH_3-cyclobutyl)CH_2-, cyclopropyl-CH_2CH_2-,
cyclobutyl-CH_2CH_2-, cyclopentyl-CH_2CH_2-, cyclohexyl-CH_2CH_2-,
(2-CH_3-cyclopropyl)CH_2CH_2-, (3-CH_3-cyclobutyl)CH_2CH_2-,
phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-,
furanyl-CH_2-, thienyl-CH_2-, pyridyl-CH_2-, 1-imidazolyl-CH_2-, oxazolyl-CH_2-,
isoxazolyl-CH_2-, phenyl-CH_2CH_2-, (2-F-phenyl)CH_2CH_2-,
(3-F-phenyl)CH_2CH_2-, (4-F-phenyl)CH_2CH_2-, furanyl-CH_2CH_2-,
thienyl-CH_2CH_2-, pyridyl-CH_2CH_2-, 1-imidazolyl-CH_2CH_2-,
oxazolyl-CH_2CH_2-, or isoxazolyl-CH_2CH_2-;

W is a bond, -CH_2-, or -$CH(CH_3)$-;

X is a bond;



Y is a bond, -CH_2-V-, -V-, or -V-CH_2-;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, -S(=O)$_2$-, -NH-, or -N(CH_3)-,

Z is phenyl 2-F-phenyl, 3-F-phenyl, 4-F-phenyl, 2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl, 2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl, 3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl, 2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl, 3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl, 3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl, 3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl, 4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl, 2-CF_3O-phenyl, 3-CF_3O-phenyl, 4-CF_3O-phenyl, furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl, 4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl, 1-benzimidazolyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino,N-piperinyl, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-, (3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, (2-MeO-phenyl)CH_2-, (3-MeO-phenyl)CH_2-, (4-MeO-phenyl)CH_2-, (2-Me-phenyl)CH_2-, (3-Me-phenyl)CH_2-, (4-Me-phenyl)CH_2-, (2-MeS-phenyl)CH_2-, (3-MeS-phenyl)CH_2-, 4-MeS-phenyl)CH_2-, (2-CF_3O-phenyl)CH_2-, (3-CF_3O-phenyl)CH_2-, (4-CF_3O-phenyl)CH_2-, (furanyl)CH_2-, (thienyl)CH_2-, (pyridyl)CH_2-, (2-Me-pyridyl)CH_2-, (3-Me-pyridyl)CH_2-, (4-Me-pyridyl)CH_2-, (1-imidazolyl)CH_2-, (oxazolyl)CH_2-, (isoxazolyl)CH_2-, (1-benzimidazolyl)CH_2-, (cyclopropyl)CH_2-, (cyclobutyl)CH_2-, (cyclopentyl)CH_2-, (cyclohexyl)CH_2-, (morpholino)CH_2-, (N-pipridinyl)CH_2-, phenyl-CH_2CH_2-, (phenyl)$_2CHCH_2$-, (2-F-phenyl)CH_2CH_2-, (3-F-phenyl)CH_2CH_2-, (4-F-phenyl)CH_2CH_2-, (2-Cl-phenyl)CH_2CH_2-, (3-Cl-phenyl)CH_2CH_2-, (4-Cl-phenyl)CH_2CH_2-, (2,3-diF-phenyl)CH_2CH_2-, (2,4-diF-phenyl)CH_2CH_2-, (2,5-diF-phenyl)CH_2CH_2-, (2,6-diF-phenyl)CH_2CH_2-, (3,4-diF-phenyl)CH_2CH_2-, (3,5-diF-phenyl)CH_2CH_2-, (2,3-diCl-phenyl)CH_2CH_2-, (2,4-diCl-phenyl)CH_2CH_2-, (2,5-diCl-phenyl)CH_2CH_2-, (2,6-diCl-phenyl)CH_2CH_2-, (3,4-diCl-phenyl)CH_2CH_2-, (3,5-diCl-phenyl)CH_2CH_2-, (3-F-4-Cl-phenyl)CH_2CH_2-, (3-F-5-Cl-phenyl)CH_2CH_2-,

(3-Cl-4-F-phenyl)CH_2CH_2-, (2-MeO-phenyl)CH_2CH_2-, (3-MeO-phenyl)CH_2CH_2-, (4-MeO-phenyl)CH_2CH_2-, (2-Me-phenyl)CH_2CH_2-, (3-Me-phenyl)CH_2CH_2-, (4-Me-phenyl)CH_2CH_2-, (2-MeS-phenyl)CH_2CH_2-, (3-MeS-phenyl)CH_2CH_2-, (4-MeS-phenyl)CH_2CH_2-, (2-CF_3O-phenyl)CH_2CH_2-, (3-CF_3O-phenyl)CH_2CH_2-, (4-CF_3O-phenyl)CH_2CH_2-, (furanyl)CH_2CH_2-, (thienyl)CH_2CH_2-, (pyridyl)CH_2CH_2-, (2-Me-pyridyl)CH_2CH_2-, (3-Me-pyridyl)CH_2CH_2-, (4-Me-pyridyl)CH_2CH_2-, (imidazolyl)CH_2CH_2-, (oxazolyl)CH_2CH_2-, (isoxazolyl)CH_2CH_2-, (benzimidazolyl)CH_2CH_2-,(cyclopropyl)CH_2CH_2-, (cyclobutyl)CH_2CH_2-,(cyclopentyl)CH_2CH_2-, (cyclohexyl)CH_2CH_2-, (morpholino)CH_2CH_2-, (N-pipridinyl)CH_2CH_2-, methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl, s-butyl, t-butyl, or allyl;

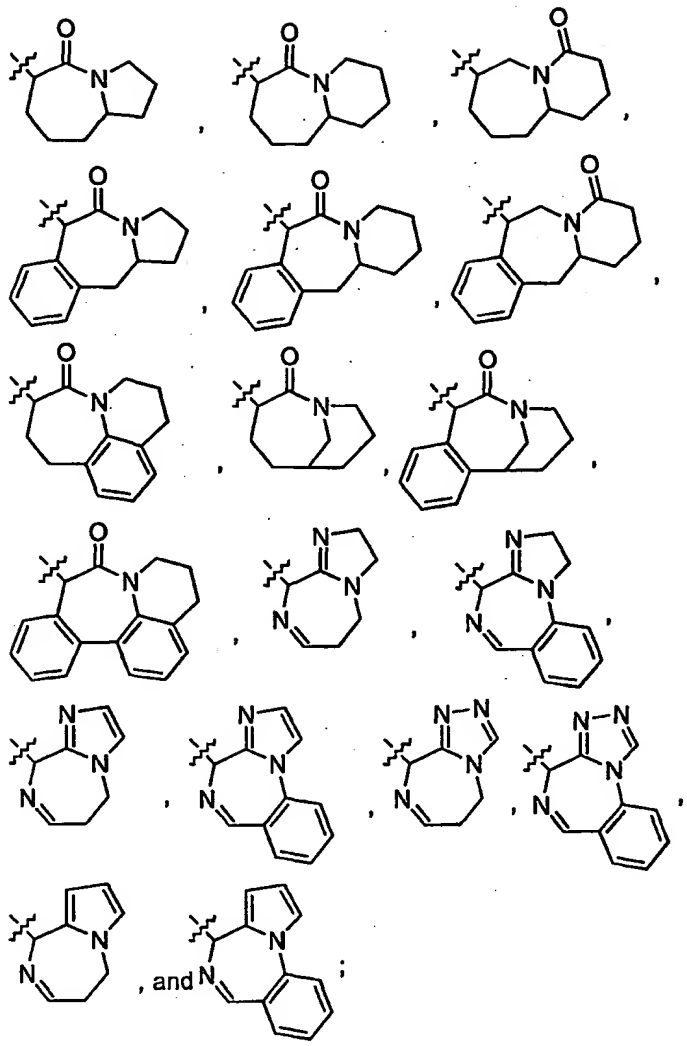
R^{10} is H, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, or (4-CF_3-phenyl)CH_2CH_2-;

R^{11}, at each occurrence, is independently selected from H, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, or (4-CF_3-phenyl)CH_2CH_2-; and

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical.

[9] In another preferred embodiment the present invention provides a compound of Formula (Ib) wherein:

ring B, along with up to 2 R^{11}s, is



wherein ring B is further substituted with 0, 1, 2, 3, or 4 R^{11}.

[10] In another preferred embodient the present invention provides a compound selected from:

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-butyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-methyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-(pyrid-2-ylmethyl)-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-(2-(diethylamino)ethyl)-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

N1-(2-benzylcarbamoyl-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-2-isobutyl-3-propyl-succinamide;

N1-[2-(1-benzyl-pyrrolidin-3-ylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide;

N1-[2-(1-benzyl-pyrrolidin-3-ylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide;

2-isobutyl-N1-[2-(4-methoxy-benzylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-3-propyl-succinamide;

2-isobutyl-N1-[2-(3-methoxy-benzylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-3-propyl-succinamide;

N1-[2-(cyclohexylmethyl-carbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide;

2-isobutyl-N1-(2-isopropylcarbamoyl-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-3-propyl-succinamide;

2-isobutyl-N1-(4-oxo-2-phenylcarbamoyl-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-3-propyl-succinamide;

(2*R*,3*S*)-3-allyl-*N*^{1}-[(7*S*)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-yl]-2-isobutylbutanediamide;

N1-(1,5-dioxo-octahydro-pyrrolo[1,2-a][1,4]diazepin-4-yl)-2-isobutyl-3-propyl-succinamide;

N1-(2-benzyloxy-5-oxo-2,3,5,6,7,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide;

N1-(2-benzyloxy-5-oxo-octahydro-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide;

N1-(2-hydroxy-5-oxo-octahydro-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide;

3-allyl-N^1-[3-(4-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(4-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1- [3-(4-benzofuran-2-yl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1- [3-(4-(4-chloro-phenyl)-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(4-(3,5-dimethylisoxazol-4-yl)phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(3-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(3-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide; and

3-allyl-N^1-[3-(3-benzofuran-2-yl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.

In another preferred embodiment of the present invention, Q is NH_2.

In another preferred embodiment

R^3 is R^4,

R^{3a} is H, methyl, ethyl, propyl, or butyl;

R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl

R^5 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl

R^{5a} is H, methyl, ethyl, propyl, or butyl; and

the total number of carbon atoms in R^3, R^{3a}, R^5 and R^{5a} equals seven or more.

In another preferred embodiment

R^3 is R^4;

R^{3a} is H;

R^4 is C_1-C_4 alkyl substituted with 1-2 R^{4a},

R^{4a}, at each occurrence, is independently selected from

C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},

phenyl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^5 is C_2-C_4 alkyl substituted with 0-3 R^{5b};

C_2-C_4 alkenyl substituted with 0-2 R^{5b}; or

C_2-C_4 alkynyl substituted with 0-2 R^{5b};

R^{5b}, at each occurrence, is independently selected from:

H, methyl, ethyl, propyl, butyl, CF_3, OR^{14}, =O;

C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};

phenyl substituted with 0-3 R^{5c}; or

5 to 6 membered heterocycle substituted with 0-2 R^{5c}; and

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy.

In another preferred embodiment

R^3 is R^4;

R^{3a} is H;

R^4 is C_2-C_4 alkyl substituted with 0-2 R^{4a},

C_2-C_4 alkenyl substituted with 0-2 R^{4a},

C_2-C_4 alkynyl substituted with 0-2 R^{4a},

R^{4a}, at each occurrence, is independently selected from is H, F, CF_3,

C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},

phenyl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^5 is C_1-C_4 alkyl substituted with 1-2 R^{5b};

R^{5b}, at each occurrence, is independently selected from:

C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};

phenyl substituted with 0-3 R^{5c}; or

5 to 6 membered heterocycle substituted with 0-2 R^{5c}; and

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy.

In another preferred embodiment

W is $-(CH_2)_p-$;

p is 1, 2, or 3;

X is a bond;

phenyl substituted with 0-2 R^{Xb};

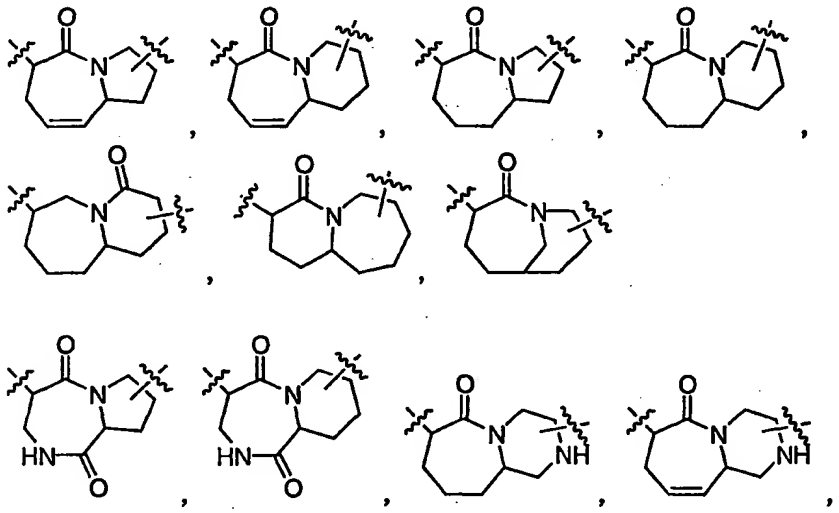
C_3-C_6 cycloalkyl substituted with 0-2 R^{Xb}; or

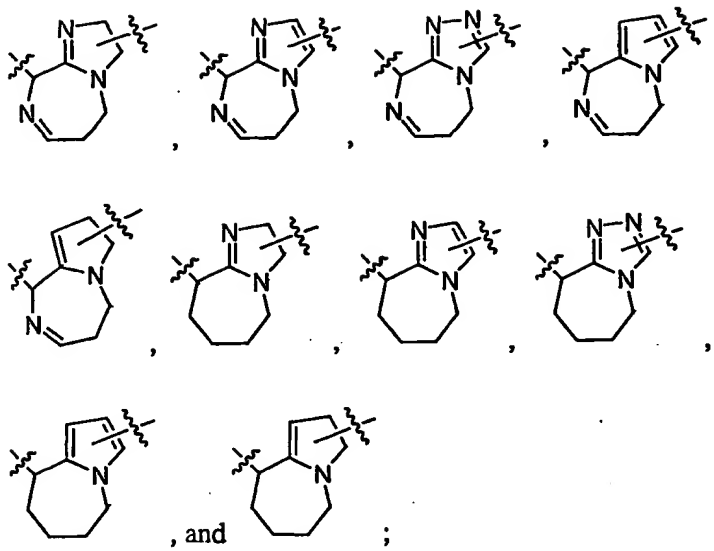
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

wherein the 5 to 6 membered heterocycle does not contain an oxo or imino substitued ring atom; and

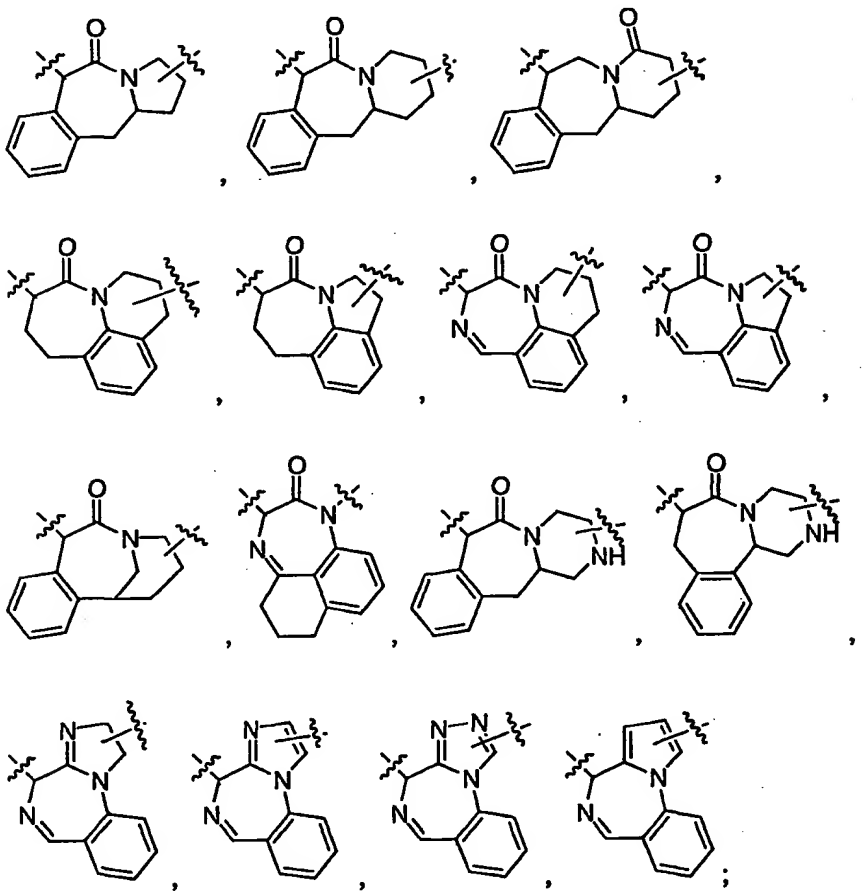
R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy.

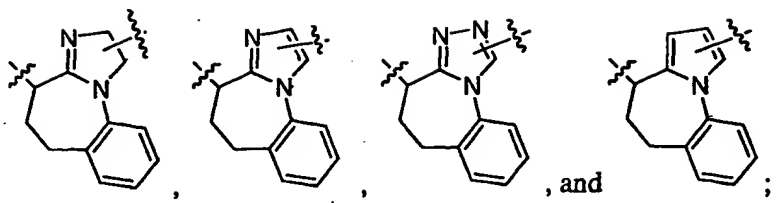
In a preferred embodiment of ring B, ring B is selected from the group consisting of a carbocyclic group of 5, 6, or 7 carbon atoms selected from -cyclopentylene-, -cyclohexylene-, -cycloheptylene-, -cyclopentenylene-, -cyclohexenylene-, and -phenylene-; a heterocycle of 5, 6, or 7 atoms selected from -pyrrolidinylene-, -piperidinylene-, -homopiperidinylene-, and -thiophenylene-; a bicyclic ring system selected from the group consisting of:



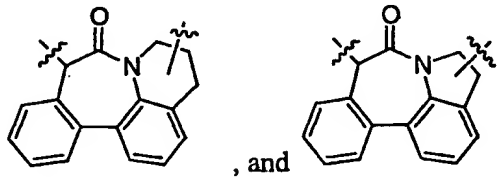


a tricyclic ring system selected from the group consisting of:



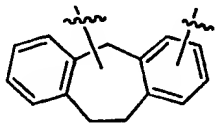


and a tetracyclic ring system selected from the group consisting of:

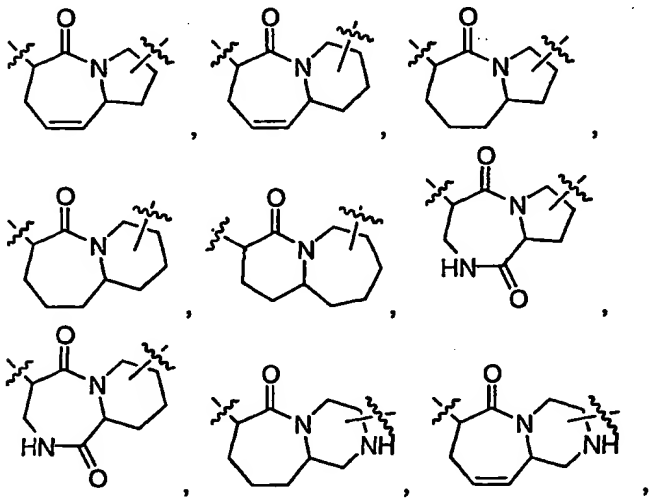


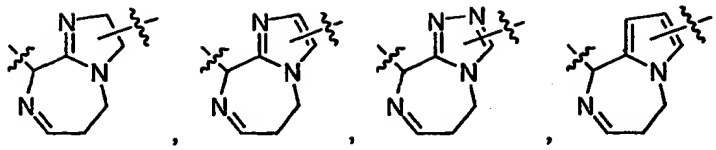
and Ring B is substituted with 0, 1, 2, 3, or 4 R^{11} groups.

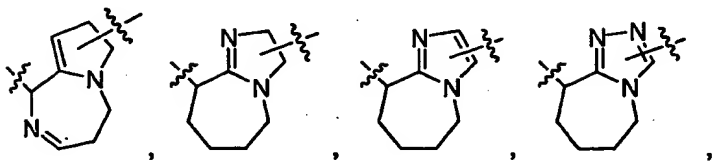
In another preferred embodiment of ring B, ring B is selected from the group consisting of -cyclopent-1,2-diyl-, -cyclopent-1,3-diyl-, -cyclohex-1,2-diyl-, -cyclohex-1,3-diyl-, -cyclohex-1,4-diyl-, -cyclohept-1,3-diyl-, -cyclopenten-3,5-diyl-, -phen-1,2-diyl-, -phen-1,3-diyl-, -phen-1,4-diyl-, -pyrrolidin-1,4-diyl-, -pyrrolidin-2,4-diyl-, -piperidin-1,4-diyl-, -piperidin-1,3-diyl-, -thiophen-2,3-diyl-, and

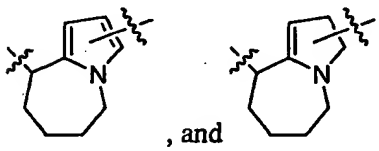


a bicyclic ring system selected from the group consisting of:

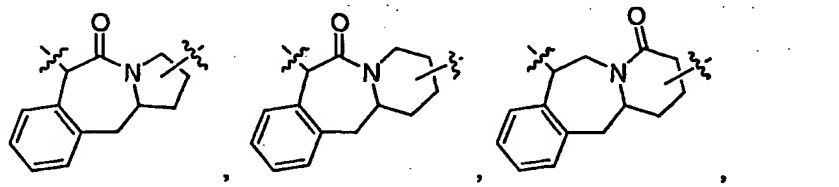


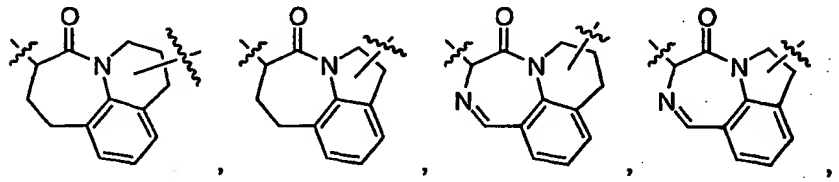


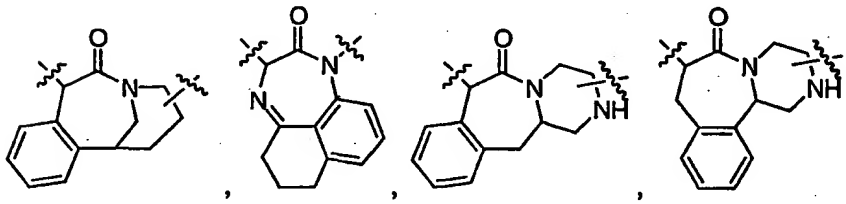


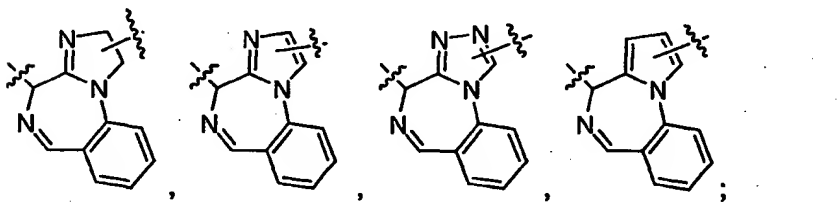

, and ;

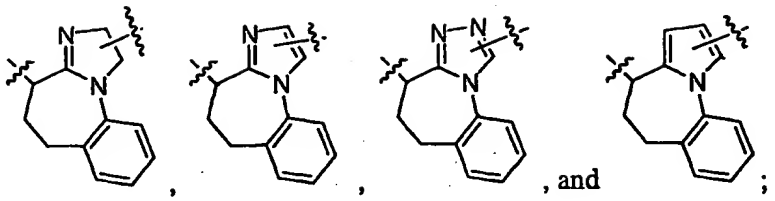
a tricyclic ring system selected from the group consisting of:



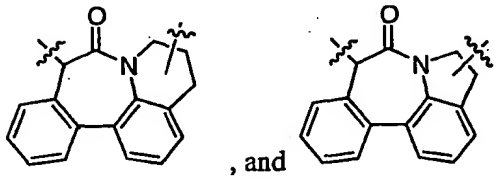





;

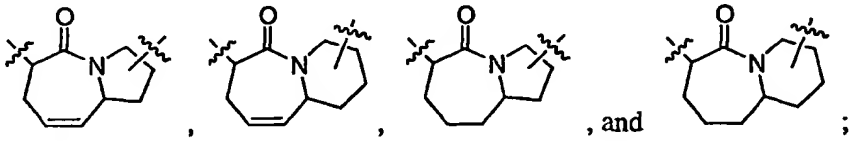


and a tetracyclic ring system selected from the group consisting of:



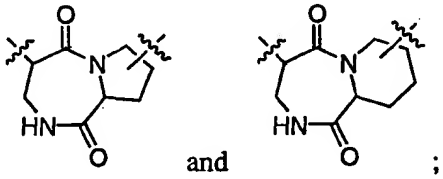
and Ring B is substituted with 0, 1, or 2 R^{11} groups.

In another preferred embodiment of ring B, ring B is selected from the group consisting of:



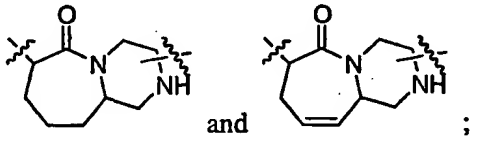
and Ring B is substituted with 0 -1 R^{11}.

In another preferred embodiment of ring B, ring B is selected from the group consisting of:



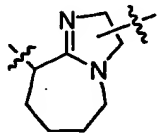
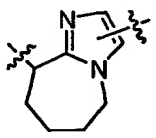
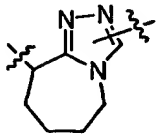
and Ring B is substituted with 0 -1 R^{11}.

In another preferred embodiment of ring B, ring B is selected from the group consisting of:



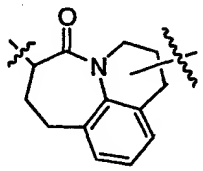
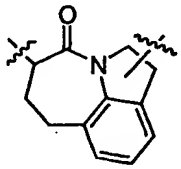
and Ring B is substituted with 0 -1 R^{11}.

In another preferred embodiment of ring B, ring B is selected from the group consisting of:


, 
, and 
;

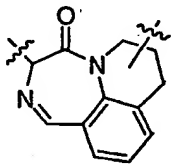
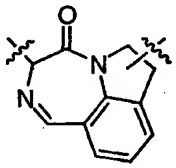
and Ring B is substituted with 0 -1 R^{11}.

In another preferred embodiment of ring B, ring B is selected from the group consisting of:


and 
;

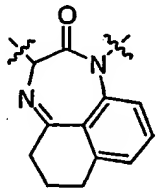
and Ring B is substituted with 0 -1 R^{11}.

In another preferred embodiment of ring B, ring B is selected from the group consisting of:


and 
;

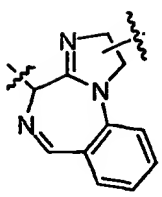
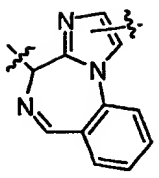
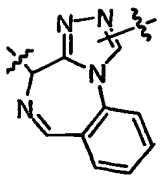
and Ring B is substituted with 0 -1 R^{11}.

In another preferred embodiment of ring B, ring B is:


;

and Ring B is substituted with 0 -1 R^{11}.

In another preferred embodiment of ring B, ring B is selected from the group consisting of:



, and

;

and Ring B is substituted with 0 -1 R^{11}.

In a preferred embodiment of R^3 and R^{3a}, R^3 is selected from C_1-C_4 alkyl, C_2-C_4 alkenyl, and C_2-C_4 alkynyl; and R^{3a} is H.

In another preferred embodiment of R^3 and R^{3a}, R^3 and R^{3a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl moiety.

In another preferred embodiment of R^3 and R^{3a}, R^3 and R^{3a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl moiety.

In another preferred embodiment of R^3, R^3 may be selected from the corresponding substituents depicted in Group B of Table 1.

In a preferred embodiment of R^5 and R^{5a}, R^5 is selected from C_1-C_4 alkyl, C_2-C_4 alkenyl, and C_2-C_4 alkynyl; and R^{5a} is H.

In another preferred embodiment of R^5 and R^{5a}, R^5 and R^{5a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl moiety.

In another preferred embodiment of R^5, R^5 may be selected from the corresponding substituents depicted in Group B of Table 1.

It is understood that any and all embodiments of the present invention may be taken in conjunction with any other embodiment to descibe additional even more preferred embodiments of the present invention.

In a second embodiment, the present invention provides a pharmaceutical composition comprising a compound of Formula (I) and a pharmaceutically acceptable carrier.

In a third embodiment, the present invention provides a method for the treatment of neurological disorders associated with β-amyloid production comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Formula (I).

In a preferred embodiment the neurological disorder associated with β-amyloid production is Alzheimer's Disease.

In a fourth embodiment, the present invention provides a method for the treatment of neurological disorders associated with β-amyloid production comprising administering to a host in need of such treatment a therapeutically effective amount of a metalloprotease inhibitor which inhibits γ secretase activity.

In a preferred embodiment the neurological disorder associated with β□amyloid production is Alzheimer's Disease.

In a preferred embodiment, the metalloprotease inhibitor is a hydroxamic acid.

In a more preferred embodiment, the metalloprotease inhibitor is a hydroxamic acid with an IC_{50} value of less than 10 μM in the Aβ immunoprecipitation assay.

In a fifth embodiment, the present invention provides a method for inhibiting γ secretase activity for the treatment of a physiological disorder associated with inhibiting γ secretase activity comprising administering to a host in need of such inhibition a therapeutically effective amount of a compound of Formula (I) that inhibits γ secretase activity.

In a preferred embodiment the physiological disorder associated with inhibiting γ secretase activity is Alzheimer's Disease.

In a sixth embodiment, the present invention provides a compound of Formula (I) for use in therapy.

In a preferred embodiment the present invention provides a compound of Formula (I) for use in therapy of Alzheimer's Disease.

In a seventh embodiment, the present invention provides for the use of a compound of Formula (I) for the manufacture of a medicament for the treatment of Alzheimer's Disease.

DEFINITIONS

As used herein, the term "Aβ" denotes the protein designated Aβ, β-amyloid peptide, and sometimes β/A4, in the art. Aβ is an approximately 4.2 kilodalton (kD) protein of about 39 to 43 amino acids found in amyloid plaques, the walls of meningeal and parenchymal arterioles, small arteries, capillaries, and sometimes, venules. The isolation and sequence data for the first 28 amino acids are described in U.S. Pat. No 4,666,829. The 43 amino acid sequence is:

1									
Asp	Ala	Glu	Phe	Arg	His	Asp	Ser	Gly	Tyr
11									
Glu	Val	His	His	Gln	Lys	Leu	Val	Phe	Phe
21									
Ala	Glu	Asp	Val	Gly	Ser	Asn	Lys	Gly	Ala
31									
Ile	Ile	Gly	Leu	Met	Val	Gly	Gly	Val	Val
41									
Ile	Ala	Thr.							

However, a skilled artisan knows that fragments generated by enzymatic degradation can result in loss of amino acids 1-10 and/or amino acids 39-43. Thus, an amino acid sequence 1-43 represents the maximum sequence of amino acids for Aβ peptide.

The term "APP", as used herein, refers to the protein known in the art as β□amyloid precursor protein. This protein is the precursor for Aβ and through the activity of "secretase" enzymes, as used herein, it is processed into Aβ. Differing secretase enzymes, known in the art, have been designated β secretase, generating the N-

terminus of Aβ, a secretase cleaving around the 16/17 peptide bond in Aβ, and "γ secretases", as used herein, generating C-terminal Aβ fragments ending at position 38, 39, 40, 41, 42, and 43 or generating C-terminal extended precursors which are subsequently truncated to the above polypeptides.

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced.

When any variable (e.g., R^{5b}) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 R^{5b}, then said group may optionally be substituted with up to two R^{5b} groups and R^{5b} at each occurrence is selected independently from the definition of R^{5b}. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein, "alkyl" or "alkylene" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms; for example, "C_1-C_6 alkyl" denotes alkyl having 1 to 6 carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, pentyl, and hexyl. Preferred "alkyl" group, unless otherwise specified, is "C_1-C_4 alkyl".

As used herein, "alkenyl" or "alkenylene" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more unsaturated carbon-carbon bonds which may occur in any stable point along the chain. Examples of "C_2-C_6 alkenyl" include, but are not limited to, ethenyl, 1-propenyl, 2-propenyl, 1-butenyl, 2-butenyl, 3-butenyl, 3-methyl-2-butenyl, 2-pentenyl, 3-pentenyl, hexenyl, and the like.

As used herein, "alkynyl" or "alkynylene" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more carbon-carbon triple bonds which may occur in any stable point along the chain, such as ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, and the like.

"Alkoxy" or "alkyloxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. Preferred alkoxy groups are methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy. Similarly, "alkylthio" or "thioalkoxy" is represents an alkyl group as defined above with the indicated number of carbon atoms attached through a sulphur bridge.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo. Unless otherwise specified, preferred halo is fluoro and chloro. "Counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, sulfate, and the like.

"Haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example $-C_vF_w$ where $v = 1$ to 3 and $w = 1$ to $(2v+1)$). Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, pentachloroethyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, heptafluoropropyl, and heptachloropropyl. "Haloalkoxy" is intended to mean a haloalkyl

group as defined above with the indicated number of carbon atoms attached through an oxygen bridge; for example trifluoromethoxy, pentafluoroethoxy, 2,2,2-trifluoroethoxy, and the like. "Halothioalkoxy" is intended to mean a haloalkyl group as defined above with the indicated number of carbon atoms attached through a sulphur bridge.

"Cycloalkyl" is intended to include saturated ring groups, having the specified number of carbon atoms. For example, "C_3-C_6 cycloalkyl" denotes such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

As used herein, "carbocycle" is intended to mean any stable 3- to 7-membered monocyclic or bicyclic or 7- to 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane (decalin), [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, or tetrahydronaphthyl (tetralin). Preferred "carbocycle" are cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

As used herein, the term "heterocycle" or "heterocyclic ring" is intended to mean a stable 5- to 7- membered monocyclic or bicyclic or 7- to 14-membered bicyclic heterocyclic ring which is saturated partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and 1, 2, 3 or 4 heteroatoms, preferably 1, 2, or 3 heteroatoms, independently selected from the group consisting of N, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom which results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. If specifically noted, a nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. It is preferred that the total number of S and O atoms in the heterocycle is not more than 1.

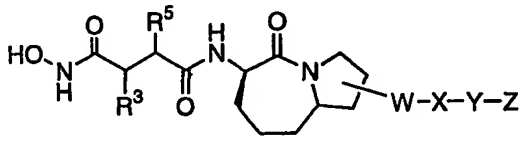
Examples of heterocycles include, but are not limited to, 1H-indazole, 2-pyrrolidonyl, 2H,6H-1,5,2-dithiazinyl, 2H-pyrrolyl, 3H-indolyl, 4-piperidonyl, 4aH-carbazole, 4H-quinolizinyl, 6H-1,2,5-thiadiazinyl, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl,

benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazalonyl, carbazolyl, 4a*H*-carbazolyl, b-carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinylperimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, piperidonyl, 4-piperidonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, xanthenyl. Preferred 5 to 10 membered heterocycles include, but are not limited to, pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl. Preferred 5 to 6 membered heterocycles include, but are not limited to, pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl; more preferred 5 to 6 membered heterocycles include, but are not limited to, pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, and tetrazolyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

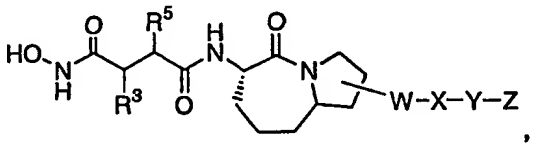
As used herein, the term "aryl", "C_6-C_{10} aryl" or aromatic residue, is intended to mean an aromatic moiety containing the specified number of carbon atoms; for example phenyl, pyridinyl or naphthyl. Unless otherwise specified, "aryl" may be unsubstituted or substituted with 0 to 3 groups selected from H, OH, OCH_3, Cl, F, Br, I, CN, NO_2,

NH_2, $N(CH_3)H$, $N(CH_3)_2$, CF_3, OCF_3, $C(=O)CH_3$, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, CH_3, CH_2CH_3, CO_2H, and CO_2CH_3.

The compounds herein described may have asymmetric centers. One enantiomer of a compound of Formula (I) may display superior biological activity over the opposite enantiomer. Both of the configurations are considered part of the invention. For example, the amino attachment to ring B may exist in either an S or R configuration. An example of such configuration includes,



and



but is not intended to be limited to this example of ring B. When required, separation of the racemic material can be achieved by methods known in the art. Additionally, the connection point of -W-X-Y-Z or other substituents to ring B may exist in two enantiomers. Both enantiomers are considered part of this invention. Additionally, the carbon atoms to which R^3 and R^5 are attached may describe chiral carbons which may display superior biological activity over the opposite enantiomer. For example, where R^3 and R^5 are not H, then the configuration of the two centers may be described as (2R,3R), (2R,3S), (2S,3R), or (2S,3S). All configurations are considered part of the invention; however, the (2R,3S) and the (2S,3R) are preferred and the (2R,3S) is more preferred.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and

animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

"Prodrugs" are intended to include any covalently bonded carriers which release the active parent drug according to formula (I) *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound of formula (I) are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of formula (I) wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug or compound of formula (I) is administered to a mammalian subject, cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited

to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of formula (I), and the like.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

SYNTHESIS

The compounds of the present invention can be prepared in a number of ways well known to one skilled in the art of organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those described below. All references cited herein are hereby incorporated in their entirety herein by reference.

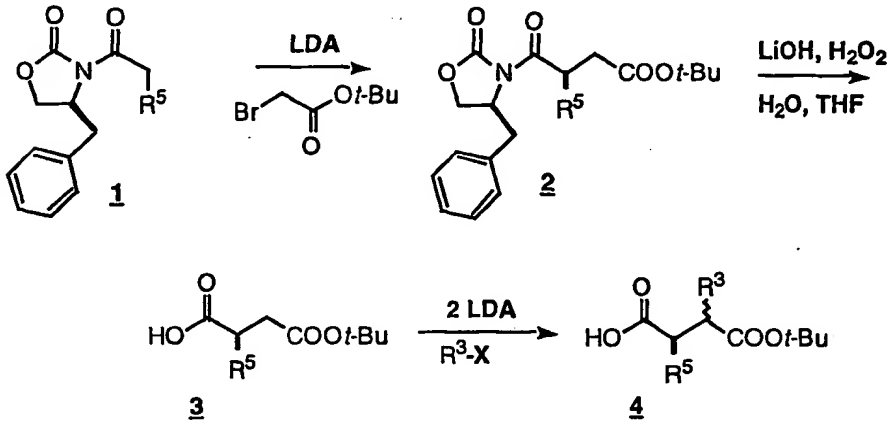
The novel compounds of this invention may be prepared using the reactions and techniques described in this section. The reactions are performed in solvents appropriate to the reagents and materials employed and are suitable for the transformations being effected. Also, in the description of the synthetic methods described below, it is to be understood that all proposed reaction conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment and workup procedures, are chosen to be the conditions standard for that reaction, which should be readily recognized by one skilled in the art. It is understood by one skilled in the art of organic synthesis that the functionality present on various portions of the molecule must be compatible with the reagents and reactions proposed. Such restrictions to the substituents which are compatible with the reaction conditions will be readily apparent to one skilled in the art and alternate methods must then be used.

Methods for the synthesis of succinylamino lactams are known in the art and are disclosed in a number of references including PCT publication number WO 96/29313, which is hereby incorporated by reference.

Disubstituted succinate derivatives can be prepared by a number of known procedures. The procedure of Evans (D. A. Evans et al, *Org. Synth.* **86**, p83 (1990)) is outlined in Scheme 1 where acylation of an oxazolidinone with an acylating agent such as an acid chloride provides structures **1**. Alkylation to form **2** followed by cleavage of

the chiral auxiliary and subsequent alkylation of the dianion of the carboxylic acid 3 provides a variety of disubstituted succinates which can be separated and incorporated into structures of Formula (I) by those skilled in the art. Additional examples are found in P. Becket, M. J. Crimmin, M. H. Davis, Z. Spavold, Synlett, (1993), 137-138, incorporated herein by reference.

Scheme 1

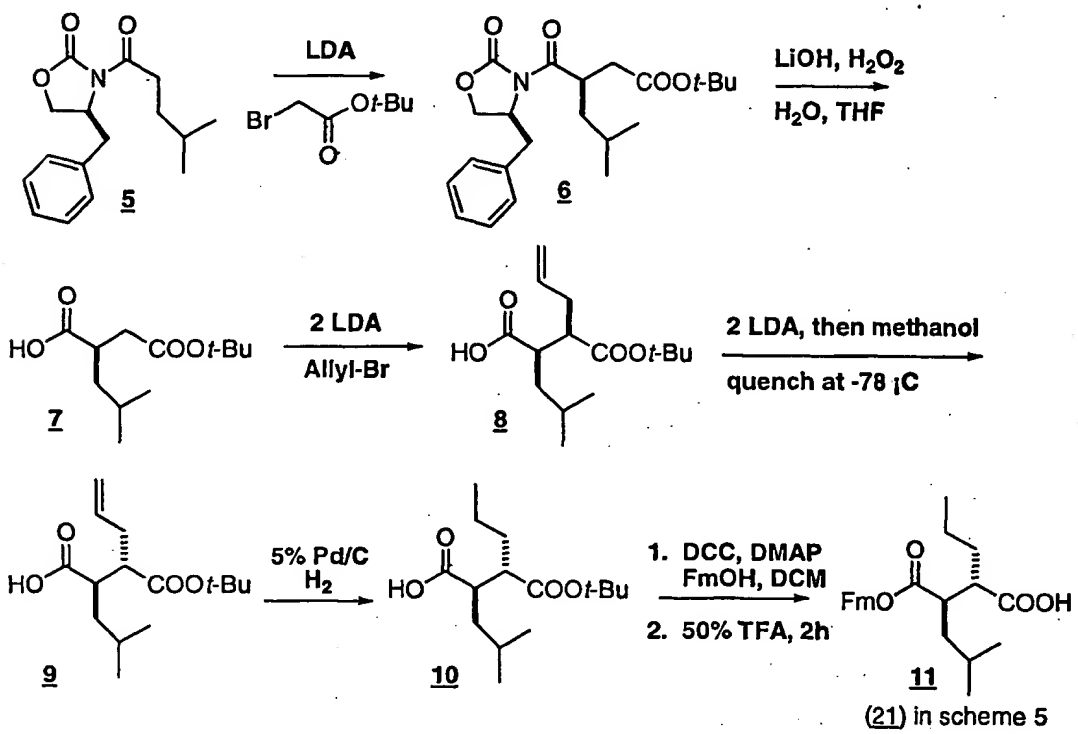


Diastereomerically pure succinate derivatives can be accessed using the chemistry outlined below, adapted from P. Becket, M. J. Crimmin, M. H. Davis, Z. Spavold, Synlett, (1993), 137-138 incorporated herein by reference. This reference provides the synthesis below to obtain compound 9. Compound 11 is used as an intermediate and is prepared from 9 by hydrogenation of the allyl group followed by coupling of 9-fluorenemethanol under standard conditions using DCC and DMAP in CH_2Cl_2. Deprotection of the *tert*-butyl ester is accomplished by treatment with 50% trifluoroacetic acid.

Additional methods useful for the preparation of succinate derivatives are known by those skilled in the art. Such references include, McClure and Axt, Bioorganic & Medicinal Chemistry Letters, 8 (1998) 143-146; Jacobson and Reddy, Tetrahedron Letters, Vol 37, No. 46, 8263-8266 (1996); Pratt et al., SYNLETT, May 1998, p. 531; WO 97/18207; and WO 98/51665. The synthetic disclosures of WO97/18207 and WO 98/51665 are hereby incorporated by reference.

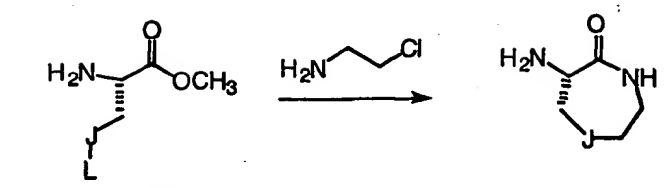
Additional methods useful for the preparation of succinate derivatives are disclosed in WO00/07995 and WO 00/38618, which are hereby incorporated in their entirety by reference.

Scheme 2



A variety of compounds of Formula (I) can be prepared by methods described in Scheme 4. The protected α amine 3 of the α amino-ε caprolactam can be prepared by methods well known in the literature for amino protecting groups as discussed in Theodora W. Greene's book "Protective Groups in Organic Synthesis", like *N*-Boc using di-*t*-butyldicarbonate in an appropriate solvent like DMSO. A sulfur atom can be introduced into the ring providing L-α amino-β thio- ε caprolactam according to the procedure in S. A. Ahmed et al, FEBS Letters, (1984), vol. 174, pages 76-9 (Scheme 3). One skilled in the art can extend this methodology to the synthesis of β amino and oxygen containing rings by analogy. The sulfur-containing molecules can also be oxidized to the sulfoxide and sulfone by methods known to one skilled in the art.

Scheme 3



J = O, S, NR^{10}

L = H

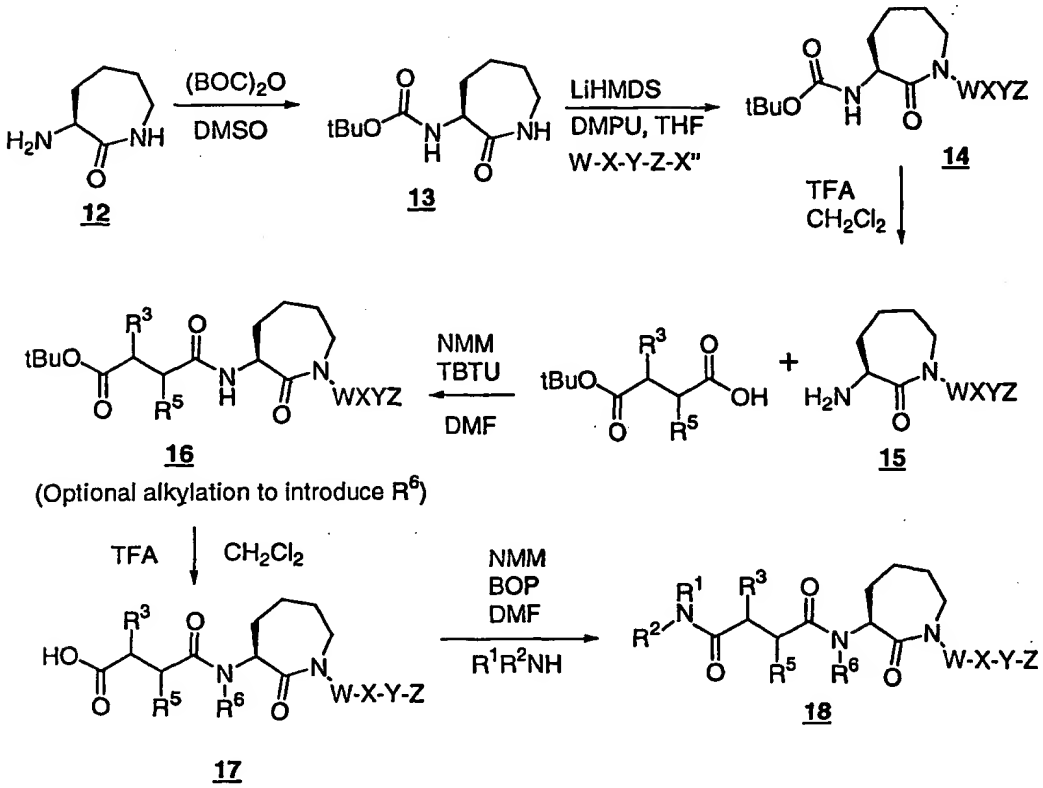
The lactam nitrogen of compound **13** can be alkylated by generating the anion with bases such as LDA, lithium bis(trimethylsilyl)amide or sodium hydride in solvents like THF, with or without cosolvents such as DMPU or HMPA and reacting this with a variety of groups containing leaving groups (X") like bromide, iodide, mesylate or tosylate. Alkylating agents such as α bromo amides, ketones and acids can be prepared by a number of literature methods including halogenation of amino acids by diazotization or are commercially available. Other suitable alkylating agents such as alkyl, allylic and benzylic halides can be formed form a variety of precursors such as free-radical addition of halides or activation of alcohols, and other chemistries known to those skilled in the art. For discussion of these types of reactions, see Carey, F.A. and Sundberg, R. J., Advanced Organic Chemistry, Part A, *New York*: Plenum Press, 1990, pages 304-305, 342-347, 695-698.

The *N*-Boc protecting group can be removed by any number of methods well known in the literature like TFA in methylene chloride to give the compound **15**. The amine **15** can be coupled to an appropriately substituted carboxylic acid or acid chloride by methods well described in the literature for making amide bonds, like TBTU in DMF with a base like NMM to give the elaborated compound **16**. Compounds **16** can be alkylated using standard bases like LDA, NaH, or NaHMDS to deprotonate the amide followed by addition of an alkylating agent with an appropriate leaving group like halide, mesylate, or triflate in an appropriate solvent to provide compounds **17** with an R^6 substituent. The *t*-butyl ester is then removed by treatment with TFA in methylene chloride to give the carboxylic acid **17**.

It is understood that methods useful for the preparation of W-X-Y-Z derivatives, on a non-commercial scale, are known by those skilled in the art or readily ascertainable from the literature. Such methods useful for the preparation of W-X-Y-Z derivatives are

disclosed in WO00/07995 and WO 00/38618, which are hereby incorporated in their entirety by reference.

Scheme 4



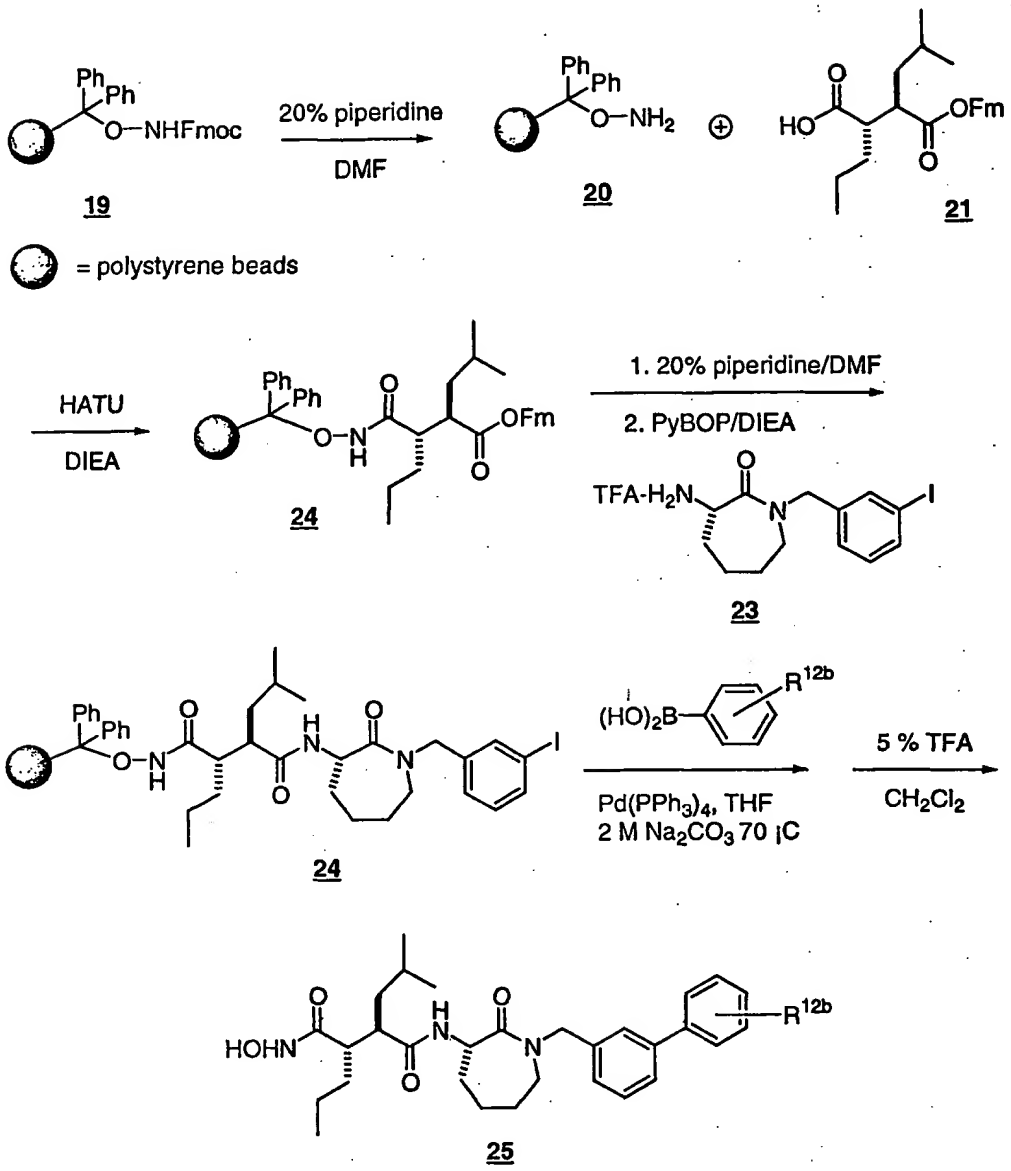
12 13 14 15 16 17 18

The final compounds 18 were prepared by treating the activated carboxylic acid of 17 with an appropriately substituted amine. For instance, activation of the carboxylic acid with HATU (*O*-(7-azabenzotriazol-1-yl)-1,1,3,3,-tetramethyluronium hexafluorophosphate) or PyBOP (benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate) or other coupling agents known to those skilled in the art allows condensation with ammonia to form primary amides. Similarly, condensation of the activated acid with hydroxylamine hydrochloride provides the hydroxamic acid, or reaction with a primary or secondary amine provides the substituted amine derivative. Activation of the acid with PyBrOP (bromo-tris-pyrrolidino-phosphonium hexafluorophosphate) followed by addition of an alcohol and 4-dimethylaminopyridine allows formation of the ester directly. For additional acylation reactions see for example

Carey, F.A. and Sundberg, R. J., Advanced Organic Chemistry, Part A, *New York*: Plenum Press, 1990, pages 475-479.

Additional Examples of compounds of Formula (I) can be prepared as shown in Scheme 5. A suitable resin for solid phase synthesis such as Fmoc (Fluorenylmethylcarbonyl)-protected hydroxylamine bound to polystyrene beads can be purchased from Novabiochem, Inc. Deprotection of the Fmoc group under standard conditions using 20% piperidine in DMF provides trityl-linked hydroxylamine resin. Coupling of a fluorenylmethyl-protected succinic acid derivative such as **20** with a coupling agent such as HATU in a suitable solvent like DMF or N-methylpyrrolidinone provides the support-bound hydroxamate **21**. The Fluorenylmethyl ester can be removed using 20% piperidine in DMF to provide the free carboxylic acid which can be coupled to amines like the caprolactam **22** (which is available using chemistry outlined in Scheme 4) using PyBOP (benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate) and a suitable base like DIEA in DMF or NMP. The support-bound intermediate **23** can then be elaborated to biaryl structures of the type **24** using typical Suzuki coupling conditions employing a catalyst such as Palladium complexes like tetrakis(triphenylphosphine)-palladium with 2M aqueous sodium carbonate as a base in a suitable solvent like THF or DME and an excess of a boronic acid. The final compounds are liberated from the support employing dilute (5%) trifluoroacetic acid in CH_2Cl_2 and purified by conventional chromatography.

Scheme 5



General procedure for solid-phase synthesis according to Scheme 5.

Resin 20 of Scheme 5: Fmoc-protected resin 19 (2.0 g, 0.78 mmol/g, 1.56 mmol) is purchased from Novabiochem and swelled in 20 ml of CH_2Cl_2 for 1 hour. The CH_2Cl_2 is removed and the resin is then treated with 25% v/v piperidine in DMF (8 mL) and allowed to shake slowly for 16 h. The solvent was removed by filtration and the resin was shaken with an additional 8 mL of 25% v/v piperidine in DMF for 2 h at room temperature. The solvents were removed by filtration, and the resin 20 was rinsed 3 x

with 20 mL of DMF, 3 x with 20 mL of methanol, and 3 x with 20 mL of CH_2Cl_2 and dried in vacuo.

Succinate 10 of Scheme 2: Succinate 9 is prepared according to the literature procedure (P. Becket, M. J. Crimmin, M. H. Davis, Z. Spavold, Synlett, (1993), 137-138; WO 97/18207; WO 98/51665). Succinate 9 (17.8 g, 66 mmol) is dissolved in 250 mL of ethyl acetate and placed in a Parr shaker bottle. To the solution is added 890 mg of 5% palladium on carbon, and the bottle is pressurized to 40 psi with hydrogen gas and shaken for 2.5 h at room temperature. The hydrogen is removed and the palladium catalyst is removed by filtration through a pad of celite. Concentration of the ethyl acetate solution provides 17.5 g (98%) of succinate 10. No further purification is necessary. MS $(M-H)^+ = 271$.

Succinate 21 of Scheme 5: Succinate 10 (6.3 g, 23.1 mmol) is dissolved in 125 mL of CH_2Cl_2 and 4.8 g (23.3 mmol) of dicyclohexylcarbodiimide is added. The solution is stirred at room temperature for 30 min and then 4.6 g (23.4 mmol) of 9-fluorenemethanol is addedfollowed by 122 mg (1 mmol) of 4-dimethylaminopyridine. After 5 h of stirring at room temperature, the reaction solution was diluted with an additional 100 mL of CH_2Cl_2 and filtered through a pad of celite to remove precipitated dicyclohexylurea. The solution was then washed 3 x with 50 mL of a 1N HCl solution, 3 x with 50 mL of a saturated sodium bicarbonate solution, and 2 x with 50 mL of brine. The crude product was dried over $MgSO_4$ and soncentrated onto 15 g of silica gel. Chromatography eluting with a gradient of 2.5% to 5% ethyl acetate/hexanes provided 6.4 g (61%) of the diester as an oil. The purified diester (6.4 g 14.2 mmol) is then dissolved in 25 mL of CH_2Cl_2 , 25 mL of trifluoroacetic acid is added, and the reaction solution is stirred at room temperature for 2 h. The reaction solution is directly concentrated *in vacuo* to an oil which is then redissolved in 25 mL of toluene and reconcentrated, followed by drying *in vacuo* to provide 6.3 g (98%) of the desired succinate 9 as an oil which solidifies on standing. MS $(M+Na)^+ = 471$, $(M+2Na)^+ = 439$.

Caprolactam 23 of Scheme 5: Boc-caprolactam 14 (5.0 g., 21.9 mmol) is dissolved in 60 mL of THF and chilled to -78°C. To the chilled solution is added 24 mL of a 1.0 M solution of lithium bis(trimethylsilyl)amide in THF, and the solution was brounght to 0°C and stirred for 15 min. To the anion solution was added 6.5 g (22

mmol) of 3-iodobenzyl bromide (Aldrich) and the the solution was allowed to warm to room temperature and stirred for 18 h. The reaction solution was diluted with 50 mL of water and extracted 3x with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by chromatography eluting with a gradient of 5-20% ethyl acetate/hexanes to afford 7.0 g (72%) of the title compound as a white solid. MS $(M+Na)^+ = 467$.

Resin 22 of Scheme 5: Resin 22 (2.0 g, 0.78 mmol/g, 1.56 mmol) was swollen in 3 mL of DMF. In a separate flask, 1.85 g (4.68 mmol) of succinate 21 was dissolved in 3 mL of DMF and 2.5 mL of *N,N*-diisopropylethylamine (14 mmol) wsa added, followed by 1.81 g (4.68 mmol) of HATU. The solution containing the active ester was added to the slurried resin and the reaction suspension was slowly shaken for 18 h. The resin was then washed 3 x with 20 mL of DMF, 3 x with 20 mL of methanol, and 3 x with 20 mL of CH_2Cl_2. Loading of the resin was determined by Fmoc quantitation to be 0.25 mmol/g, see Reddy, M. P.; Voelker, P.J. *Int. J. Pept. Protein Res.* 1998, 31, 345-348.

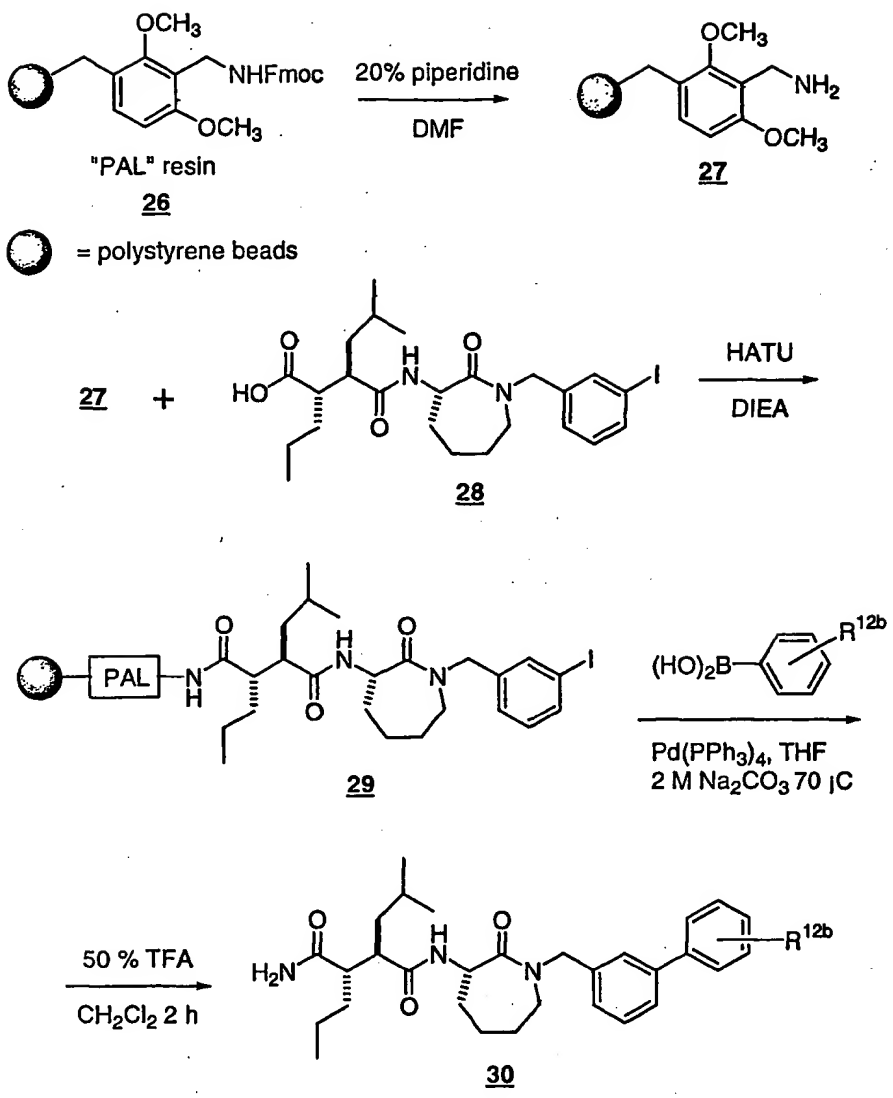
Resin 24 of Scheme 5: Resin 22 (2.0 g , 0.25 mmol/g, 0.5 mmol) was suspended in 10 mL of 25% piperidine in DMF. The suspended resin was shaken for 30 min at room temperature, and then the resin was washed 3 x with 20 mL of DMF, 3 x with 20 mL of methanol, and 3 x with 20 mL of CH_2Cl_2. Deprotected resin (1.0 g, 0.25 mmol) was swollen in 2 mL of DMF. To the slurry was added 650 mg (1.25 mmol) of PyBOP and 217 mL (1.25 mmol) of DIEA. Separately, 443 mg (0.97 mmol) of caprolactam 23 was dissolved in 2 mL of DMF and 436 mL (2.5 mmol) of DIEA was added. The caprolactam solution was added to the resin slurry and the resin was mixed for 18 h at room temperature. The solvents were then removed and the coupling was repeated, with shaking at room temperature for 6 h. The resin was then washed 3 x with 10 mL of DMF, 3 x with 10 mL of methanol, and 3 x with 10 mL of CH_2Cl_2.

Products 25 of Scheme 5: A 70 mg (17.5 mmol) portion of resin 24 was suspended in 1 mL of THF in a screw-cap vial. To the slurry was added a boronic acid (0.15 mmol), 150 mL of a 2 M solution of sodium carbonate, and 15 mg (13 mmol) of tetrakis(triphenylphosphine)palladium. The vial was tightly closed and heated to 60°C for 16 h using a dry heater on a shaker table. The solvents were then removed by filtration and the resin was washed 3 x with THF (2 mL), 3 x with methanol (2 mL), 3 x

with water, and 3 x with CH_2Cl_2. The resins were then placed in a glass vial and cleaved with 1 mL of 5% trifluoroacetic acid in CH_2Cl_2 for 30 min. The solution ws filtered off and the resin was washed with an additional 2 mL of CH_2Cl_2 and the combined filtrates were evaporated to dryness to yield the crude products **25**. The products were purified by chromatography eluting with 10-100% ethyl acetate in hexanes to yield 13.0 to 6.0 mg (14-60%) of the final products.

Additional Examples of compounds of Formula (I) can be prepared as shown in Scheme 6. A suitable resin for solid phase synthesis such as Fmoc (Fluorenylmethylcarbonyl)-protected peptide amide linker (PAL)-derivatized polystyrene beads can be purchased from Perkin Elmer Biosystems, Inc. Deprotection of the Fmoc group under standard conditions using 20% piperidine in DMF provides the free benzylamine. Coupling of a succinic acid derivative such as **28** (which is available using chemistry outlined in Scheme 4) with a coupling agent such as HATU in a suitable solvent like DMF or N-methylpyrrolidinone provides the support-bound amide **29**. The support-bound intermediate **29** can then be elaborated to biaryl structures of the type **24** using typical Suzuki coupling conditions employing a catalyst such as Palladium complexes like tetrakis(triphenylphosphine)-palladium with 2M aqueous sodium carbonate as a base in a suitable solvent like THF or DME and an excess of a boronic acid. The final compounds are liberated from the support employing 50% trifluoroacetic acid in CH_2Cl_2 and can be purified by conventional chromatography or preparative HPLC.

Scheme 6



General procedure for solid-phase synthesis according to Scheme 6

Resin 27 of Scheme 6: Fmoc-protected PAL resin 26 (0.80 g, 0.50 mmol/g, 0.40 mmol) is purchased from Advanced Chemtech and swelled in 20 ml of CH_2Cl_2 for 1 hour. The CH_2Cl_2 is removed and the resin is then treated with 25% v/v piperidine in DMF (6 mL) and allowed to shake slowly for 1 h. The solvents were removed by filtration, and the resin 27 was rinsed 3 x with 20 mL of DMF, 3 x with 20 mL of methanol, and 3 x with 20 mL of CH_2Cl_2. and dried in vacuo.

Acid 28 of Scheme 6: To a solution of 0.100 g (367 mmol) of succinate 10 dissolved in 2.0 mL of dry DMF was added 0.120 mL (1.10 mmol) of N-

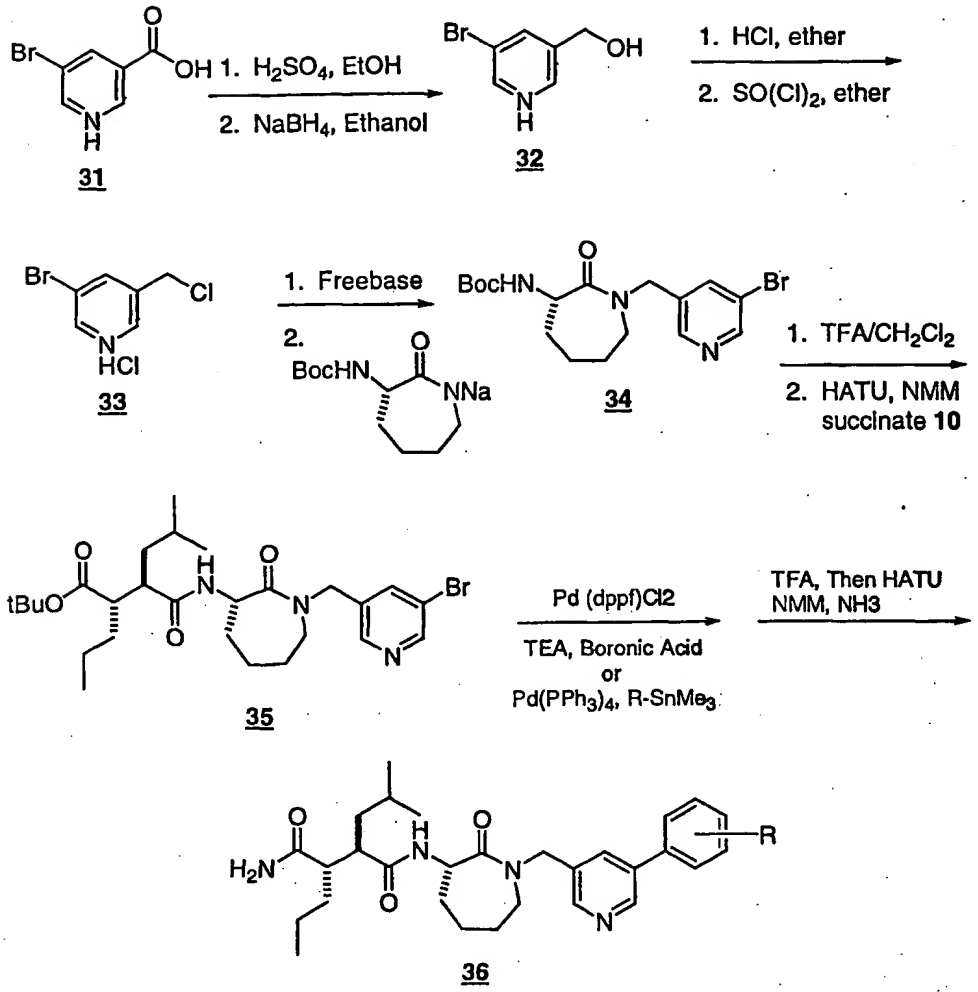
methylmorpholine. A second solution containing 0.139 g (0.403 mmol) of caprolactam 23 of Scheme 5 dissolved in 2.0 mL of DMF was then added. To the mixed solution was added 229 mg (0.440 mmol) of PyBop and the reaction solution was stirred for 16 h at room temperature. The reaction solution was diluted with water (20 mL) and extracted 3 x with 100 mL of ethyl acetate. The combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The resulting oil was purified by chromatography eluting with a gradient of 5-20% ethyl acetate in hexanes to provide 0.195 g (0.360 mmol, 98%) of the *tert*-butyl ester of Acid 28 (MS M+Na= 621). The purified ester (0.195 g, 0.360 mmol) was dissolved in 10 mL of 25% trifluoroacetic acid in CH_2Cl_2 and stirred for 2 h at room temperature. The solvents were removed under reduced pressure and the acid was redissolved in 5 mL of toluene and reconcentrated 2 x to remove residual TFA. The crude acid was found to be pure by ^1H NMR and was used in Scheme 6 without further purification.

Resin 29 of Scheme 6. Resin 27 (800 mg, 0.40 mmol) was solvated in 4.0 mL of dry DMF and and 0.63 mL (3.6 mmol) of diisopropylethylamine was addedfollowed by a solution of Acid 28 dissolved in 4 mL of DMF. To the slurry was then added 0.465 g (1.2 mmol) of HATU and the slurry was shaken for 26 h at room temperature. The solvents were removed by filtration, and the resin 29 was rinsed 3 x with 20 mL of DMF, 3 x with 20 mL of methanol, and 3 x with 20 mL of CH_2Cl_2. and dried in vacuo.

Products 30 of Scheme 6: A 75 mg (0.38 mmol/g, 28.8 mmol) portion of resin 24 was suspended in 1 mL of THF in a screw-cap vial. To the slurry was added a boronic acid (0.33 mmol), 150 mL of a 2 M solution of sodium carbonate, and 15 mg (13 mmol) of tetrakis(triphenylphosphine)palladium. The vial was tightly closed and heated to 60°C for 16 h using a dry heater on a shaker table. The solvents were then removed by filtration and the resin was washed 3 x with THF (2 mL), 3 x with methanol (2 mL), 3 x with water, and 3 x with CH_2Cl_2 . The resins were then placed in a glass vial and cleaved with 1 mL of 5% trifluoroacetic acid in CH_2Cl_2 for 2 h. The solution was filtered off and the resin was washed with an additional 2 mL of CH_2Cl_2 and the combined filtrates were evaporated to dryness to yield the crude products 25. The products were purified by chromatography eluting with 10-100% ethyl acetate in hexanes to yield 0.5 to 2.0 mg (14-60%) of the final products.

The internal phenyl ring can be exchanged for a pyridine ring using chemistry outlined in Scheme 7. The chloromethyl pyidine 33 is prepared using a known procedure reported in Nutaitis, Charles F.; Ledeboer, Mark W. Org. Prep. Proced. Int. (1992), 24(2), 143-6 Incorporated herein by reference. After freebasing the pyridine, alkylation with the Boc-caprolactam provides pyridine intermediate 34, which can be elaborated to the protected amide 35 with succinate 10. Substitution can then be introduced using Suzuki methodology employing a palladium source such as tetrakis(triphenylphosphine) palladium(0) or bis(diphenylphosphinoferrocene) palladium(II) dichloride and a suitable base such as sodium carbonate or triethylamine in a solvent such as THF or toluene containing 10% methanol. Stille chemistry is also possible using a suitable palladium source such as tetrakis(triphenylphosphine)palladium(0) and an aryl or vinyl tin derivative in a solvent such as benzene, toluene, or xylenes. The tert-butyl ester is then deprotected under standard acidic conditions using trifluoroacetic acid and the amide is formed under standard conditions to provide products 36.

Scheme 7



General procedure for synthesis according to Scheme 7

The chloromethyl pyidine HCl salt 33 is prepared using a known procedure reported in Nutaitis, Charles F.; Ledeboer, Mark W. Org. Prep. Proced. Int. (1992), 24(2), 143-6.

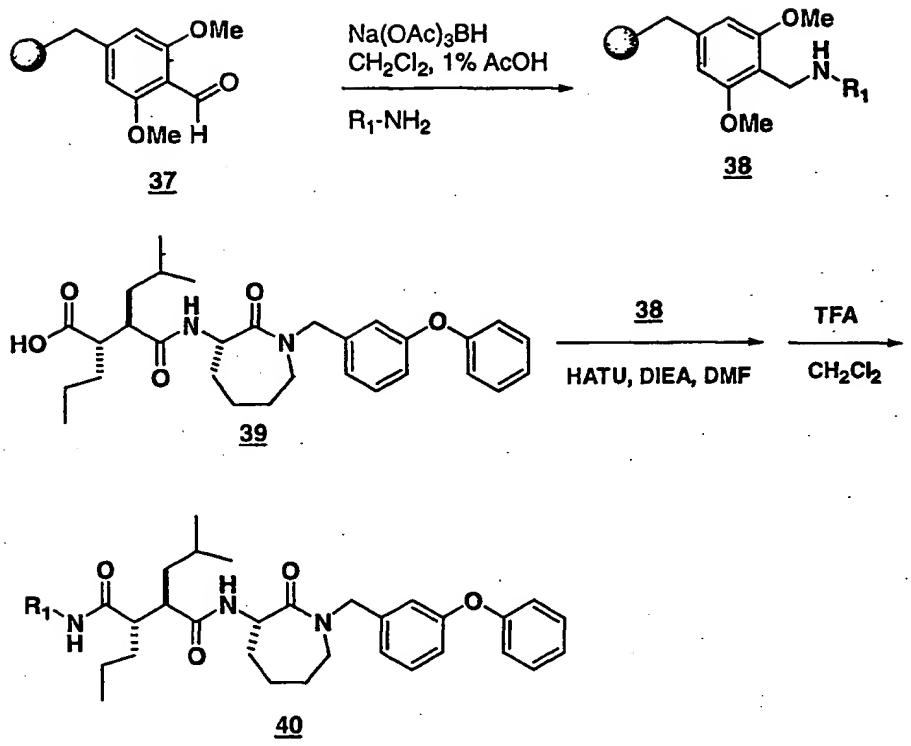
Caprolactam 34: Pyridine HCl salt 33 (2.0 g, 8.3 mmol) is dissolved in 50 mL of a saturated $NaHCO_3$ solution and the solution is extracted with 30 mL of CH_2Cl_2 3 x followed by concentration of the organic layers to provide the free base. Separately, 1.8 g (7.8 mmol) of caprolactam 13 is dissolved in 40 mL of dry THF and chilled to -78 °C. To the solution was added 8.7 mL of a 1M solution of sodium bis(trimethylsilyl) amide. The solution was brought to 0°C and stirred for 30 min. To the resultant anion was added a solution of 1.7 g (8.3 mmol) of pyridine 33 free base dissolved in 40 mL of THF. The resulting reaction solution was stirred at room temperature for 18 h and then

heated to 50 °C and stirred an additional 3 h. The reaction solution was allowed to cool and then 50 mL of water was added and the aqueous layer was extracted 2 x with 100 mL of ethyl acteate. The combined organic layers were dried and concentrated under reduced pressure to provide the crude product which was purified by chromatography eluting with 20 to 100% ethyl acetate in hexanes to provide 1.5 g (51%) of caprolactam 34 as an oil.

Amide 35: Caprolactam 34 (0.40 g, 1.0 mmol) is dissolved in 20 mL of 50% trifluoroacetic acid in CH_2Cl_2 and stirred at room temperature for 30 min. The solvents were then removed under reduced pressure and the resulting oil was redissolved in 5 mL of toluene and reconcentrated to remove residual TFA. Separately, 0.270 g (1.0 mmol) of succinate 10 was dissolved in 5.0 mL of dry DMF and 0.44 mL (4 mmol) of *N*-methylmorpholine was added followed by 0.50 g (1.3 mmol) of HATU and the resulting solution was stirred at room temperature for 30 min. The crude deprotected caprolactam from above was dissolved in 5.0 mL of dry DMF and added to the succinate solution and the resulting solution was heated to 50 °C and stirred for 2 days. The solution was then diluted with 20 mL of water and extracted with 3 50 mL portions of ethyl acetate. The combined organic layers were dried and concentrated under reduced pressure to provide an oil which was purified by chromatography eluting with 20 to 50% ethyl acetate in hexanes to provide 0.40 g (70%) of the Amide 35.

Additional examples can be prepared by the method shown in Scheme 8. Coupling of an amine onto a commercially available aldehyde-derived resin 37 under conditions for reductive amination such as sodium tris(acetoxy)borohydride in CH_2Cl_2 containing 1% acetic provides a support-bound amine 38. The carboxylic acid 39 can then be coupled to the support-bound amine generating an amide 40 which can be liberated from the support employing trifluoroacetic acid in CH_2Cl_2.

Scheme 8



General procedure for solid-phase synthesis according to Scheme 8

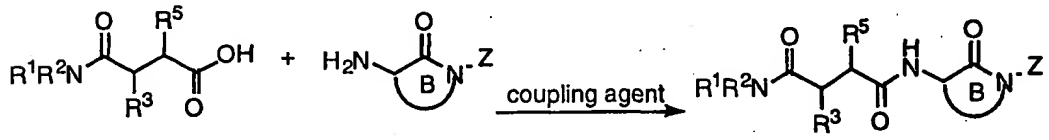
Resin 38 of Scheme 5: Aldehyde-derived resin 37 (200 mg, 0.5 mmol/g, 0.1 mmol) is purchased from Perkin Elmer Biosystems and swelled in 3 ml of CH_2Cl_2 for 1 hour. An amine (1.0 mmol), sodium tris(acetoxy)borohydride (106 mg, 0.5 mmol) and acetic acid (30 uL, 1%) are added and the reaction is shaken on a shaker table for 16 h at room temperature. The solvents were removed by filtration and the resin 38 was rinsed 3 x with 20 mL of DMF, 3 x with 20 mL of methanol, and 3 x with 20 mL of CH_2Cl_2. and dried in vacuo.

Products 40 of Scheme 8: Carboxylic acid 39 (23 mg, 0.045 mmol), diisopropylethylamine (13 mL, 0.075 mmol) and HATU (17.1 mg, 0.045 mmol) were mixed in 0.5 mL of DMF for 30 min. Amine-derived resins 38 (30 mg, 0.015 mmol) were then added and the suspension was shaken at room temperature for 16 h.. The solvents were removed by filtration and the resins were rinsed 3 x with 20 mL of DMF, 3 x with 20 mL of methanol, and 3 x with 20 mL of CH_2Cl_2. The isolated resins were then cleaved by the addition of 0.50 mL of trifluoroacetic acid. The product solutions were concentrated and redissolved in 0.5 mL of methanol and reconcentrated 2x to

remove residual TFA. Product yields ranged from 0-100% based on the structure of the amine.

The compounds of Formula (I) of the present invention can also be prepared from aminolactam 42 and succinic acid derivatives 41 using amide bond syntheses known in the art, including methods commonly used in peptide syntheses, such as HATU, TBTU, BOP, pyBOP, EDC, CDI, DCC, hydroxysuccinimide, mixed carboxylic anhydride, and phenyl ester mediated couplings, as illustrated in Scheme 9 for the synthesis of aminolactam 43, an embodiment of the present invention.

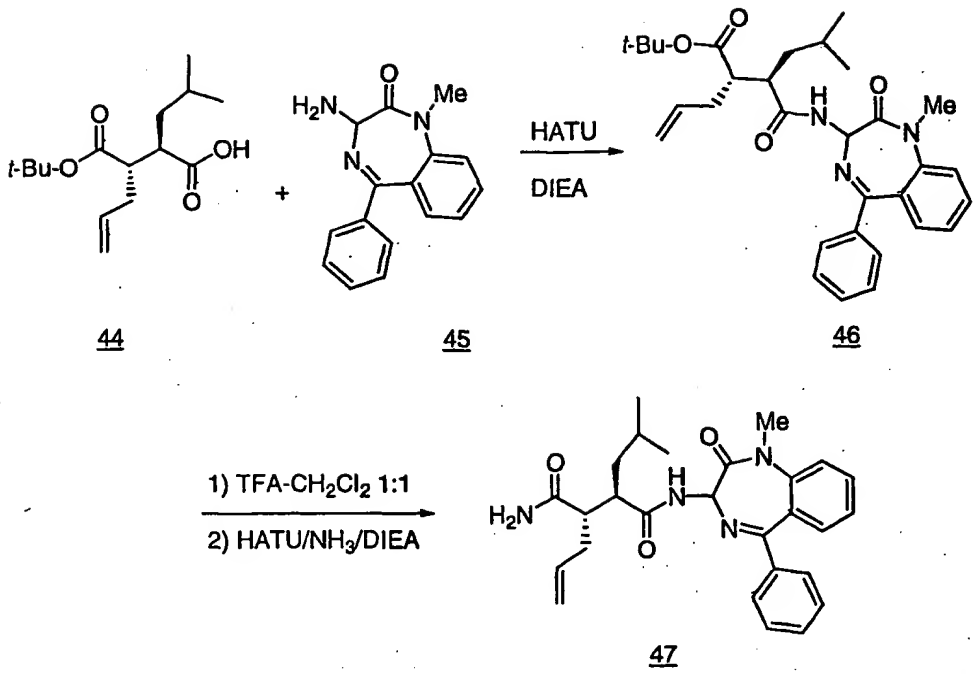
Scheme 9



41 42 43

Depending on the structure of the final product, it is appreciated by those skilled in the art that protecting groups or precursor functionality convertable to the desired groups may be desireable. Protecting groups and their use in synthesis are described in Green and Wuts, *Protective Groups in Organic Synthesis*, (Wiley 1991). The use of protecting groups is further illustrated in Scheme 10, in which the succinate half-ester 44 (Becket et al., Synlett 1993, 137-138) is coupled to the aminobenzodiazepine 45 (Sherrill and Sugg, J. Org. Chem. 1995, 60, 730-734; Bock et al., J. Med. Chem., 1993, 36, 4276-4292) to give ester 46, followed by conversion of the ester group to the primary amide 47.

Scheme 10



44 45 46

47

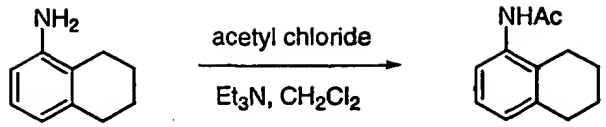
Methods for the synthesis of lactams as contemplated by the present invention in lactam ring B in Formula (I), including amino benzodiazepines, are known in the art and are disclosed in a number of references including PCT publication number WO 98/28268, which is hereby incorporated by reference. Additional references include Bock, et al, J. Org. Chem., **1987**, *52*, 3232-3239 and Sherrill et al, J. Org. Chem., **1995**, *60*, 730-734; Walsh, D. A., Synthesis, September 1980, p.677.

The carbocyclic and heterocyclic B groups can be synthesized using methods described in WO 98/28268, WO99/32453, and WO/99/67221 and references cited therein. The synthetic disclosures of WO 98/28268, WO99/32453, and WO/99/67221, and the references which are cited within these references, are hereby incorporated by reference.

EXAMPLES

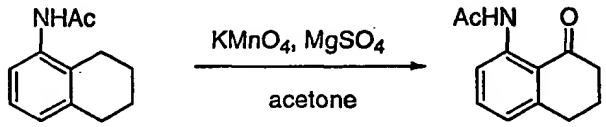
Example 1

Representative procedure for 4-butyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepine core 1.



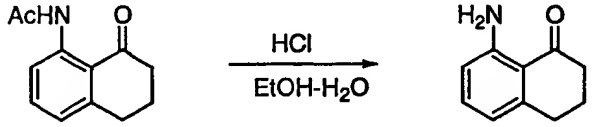
1-1 **1-2**

5,6,7,8-Tetrahydro-1-naphthylamine (**1-1**, 24.0 g, 163 mmol) and triethylamine (33.4 g, 330 mmol) were dissolved in CH_2Cl_2 (120 mL). The solution was cooled to 0° C in an ice-water bath. Acetyl chloride (19.5 g, 248 mmol) was added dropwise over 30 min. The reaction mixture was warmed to room temperature. After the solvent was removed *in vacuo*, the slurry was filtered. The solid was washed with water and dried under high vacuum to provide **1-2** (28.68 g, 93% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 7.7 Hz, 1 H), 7.12 (t, J = 7.7 Hz, 1 H), 6.94 (m, 2 H), 2.78 (t, J = 6.1 Hz, 2 H), 2.59 (t, J = 6.0 Hz, 2 H), 2.20 (s, 3 H), 1.80 (m, 4 H). [M. Sugimori et al J. Med. Chem. 1998, 41, 2308]



1-2 **1-3**

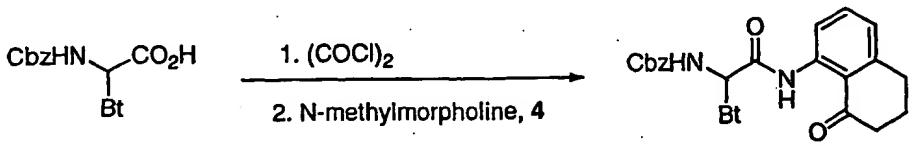
To a solution of **1-2** (28.0 g, 148 mmol) in a mixture of acetone (1.5 L) and 15% aqueous $MgSO_4$ (133 mL) was added $KMnO_4$ (70.0 g, 444 mmol) in portions at 0°C. The reaction mixture was stirred for 12 h at room temperature and diluted with water. After removal of the volatile *in vacuo*, the mixture was extracted with CH_2Cl_2, and the organic phase was washed successively with saturated $NaHSO_3$, 1 N NaOH, brine and dried ($MgSO_4$). Evaporation of the solvent provided **1-3** as a yellow solid (17.0 g, 57 % yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, J = 8.4 Hz, 1 H), 7.44 (t, J = 8.0 Hz, 1 H), 6.92 (d, J = 7.7 Hz, 1 H), 2.97 (t, J = 6.0 Hz, 2 H), 2.70 (t, J = 6.6 Hz, 2 H), 2.23 (s, 3 H), 2.09 (m, 2 H).



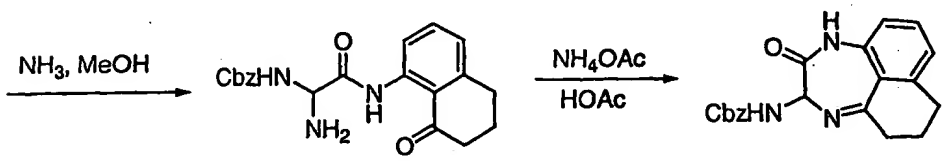
1-3 **1-4**

A solution of **1-3** (17.0 g, 83.6 mmol) in a mixture of EtOH (150 mL) and 6 N HCl (70 mL) was heated to 100° C for 6 h. After the reaction mixture was cooled to room temperature, it was neutralized with NaOH to pH = 13 and extracted with EtOAc. The organic layer was washed with brine, dried (Na_2SO_4) and evaporated. Flash column

chromatography (10% EtOAc/hexane) of the reside gave **1-4** (10.0 g, 42.0 % yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (t, J = 8.0 Hz, 1 H), 6.46 (m, 4 H), 2.87 (t, J = 6.0 Hz, 2 H), 2.63 (t, J = 6.6 Hz, 2 H), 2.04 (m, 2 H); MS (ESI, MH) 162.2.



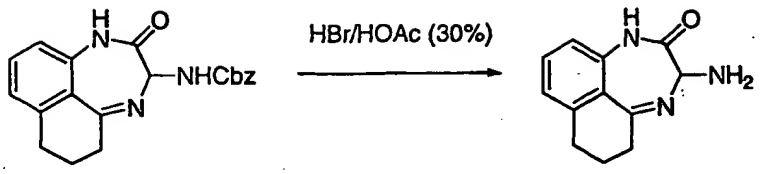
1-5 **1-6**



1-7 **1-8**

A solution of 2-(benzotriazol-1-yl)-N-(benzyloxycarbonyl)glycine (**1-5**, 22.25 g, 68.2 mmol) in anhydrous THF (200 mL) and CH_2Cl_2 (35 mL) under N_2 was cooled to 0° C with an ice-water bath. Oxalyl chloride (8.66 g, 68.2 mmol) was added followed by anhydrous DMF (0.2 mL). After maintaining the reaction mixture at 0 – 5° C for 2 h, a solution of **1-4** (10.0 g, 62.0 mmol) and N-methylmorpholine (13.8 g, 136 mmol) in THF (80 mL) was added dropwise over 30 min. The mixture was allowed to warm to room temperature and the reaction slurry was filtered. The solid was washed with minimum amount of cold THF. The mother liquor containing **1-6** was saturated with ammonia gas and stirred overnight. Following solvent displacement into $CHCl_3$, the solution of crude **1-7** was washed with 1 N NaOH, brine, dried ($MgSO_4$) and concentrated *in vacuo*.

The crude **1-7** was dissolved in glacial acetic acid (300 mL), combined with ammonium acetate (15.0 g), was stirred at room temperature overnight. The reaction mixture was concentrated and suspended in EtOAc and Et_2O. Aqueous NaOH was added until the pH > 9. The resulting slurry was cooled to 0 – 5° C in an ice-water bath and then filtered. The solid was washed consecutively with water and Et_2O and dried under high vacuum to provide **1-8** (12.5 g, 53 % yield) as a crystalline solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (br s, 1 H), 7.25 – 7.45 (m, 6 H), 7.05 (d, J = 7.3 Hz, 1 H), 6.92 (d, J = 8.1 Hz, 1 H), 6.54 (d, J = 8.4 Hz, 1 H), 5.05 – 5.30 (m, 3 H), 2.65- 3.00 (m, 4 H), 2.05 – 2.20 (m, 1 H), 1.90 – 2.05 (m, 1 H); MS (ESI, MH) 350.4.

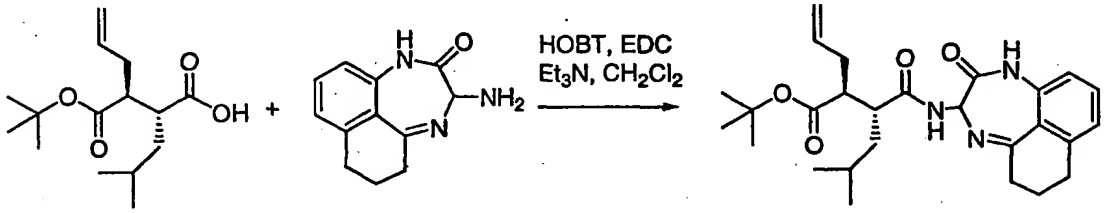


1-8 core 1

1-8 (2.0 g, 5.7 mmol) was dissolved in HBr/HOAc (30%, 30 mL) and stirred for 5 h at ambient temperature. The reaction mixture was then diluted with ether (200 mL). The precipitate was filtered under nitrogen atmosphere and washed thoroughly with ether to give a yellow solid. The solid was dissolved in H_2O, saturated with K_2CO_3, and extracted with ethyl acetate. The organic phase was dried (Na_2SO_4). Evaporation of the solvent gave **core 1** (900 mg, 73%) as a yellow solid. MS *m/z* 216.1 (MH^+).

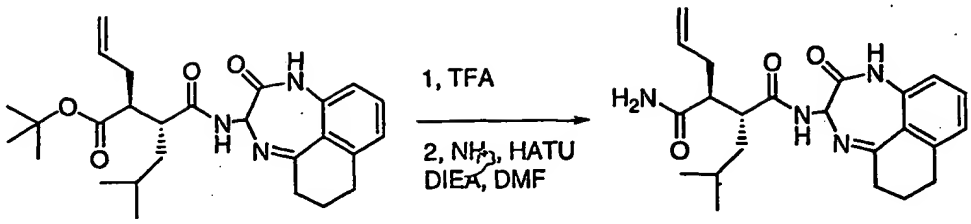
Example 1a

Representative procedure: (2R, 3S)-3-allyl-2-isobutyl-N^1-(4-butyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide (Example **1a**)



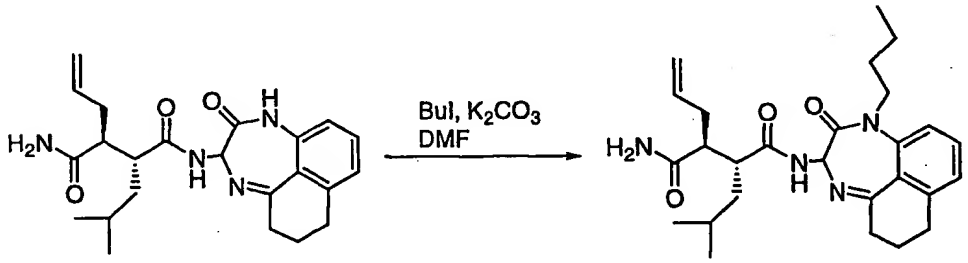
1-10 1-9 1-11

1-9 (880 mg, 4.10 mmol), **1-10** (1.10 g, 4.10 mmol), 1-hydroxybenzotriazole hydrate (HOBT, 665 mg, 4.92 mmol) were suspended in CH_2Cl_2, and cooled to 0° C. 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC–HCl, 1.18 g, 6.15 mmol) and triethylamine (0.86 mL, 6.15 mmol) were added subsequently. After being stirred for 24 h at ambient temperature, the reaction mixture was diluted with ethyl acetate. The organic layer was washed with water, brine and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified on silica gel (5% methanol/methylene chloride) to afford **1-11** (1.51 g, 79%). MS *m/z* 468.5 (MH^+).



1-11 1-12

1-11 (1.93 g, 4.10 mmol) was dissolved in CH_2Cl_2/TFA (8 mL, 1:1) and stirred for 4 h at ambient temperature. Solvent was removed by rotovap, and the residue was dissolved in DMF (10 mL) and cooled to 0 °C. To the above solution was added HATU (1.87 g, 4.90 mmol), diisopropylethylamine (0.26 mL, 6.15 mmol) and bubbled with anhydrous ammonia for 20 min. Stirring was continued overnight. DMF was removed *in vacuo*, the residue was diluted with ethyl acetate, washed with water, brine, and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified on silica gel (5% methanol/methylene chloride) to afford product **1-12** (745 mg, 44%) as a white solid. MS *m/z* 411.3 (MH^+).



1-12 1-13

A mixture of **1-12** (410.5 mg, 1.0 mmol), iodobutane (552.1 mg, 3.0 mmol), and potassium carbonate (276.4 mg, 2.0 mmol) in anhydrous DMF (3 mL) was stirred at ambient temperature for 20 h. The reaction mixture was diluted with ethyl acetate. The organic layer was washed with 5% aqueous LiCl, brine, and dried ($MgSO_4$). Fter the solvent was evaporated, the residue was purified on silica gel (3% methanol/methylene chloride) to provide **1-13** (384 mg, 82%) as a white solid. This mixture of two diastereoisomers was separated on chiral AD column with methanol/isopropanol/hexane to give Example **1a'** and Example **1a"**.

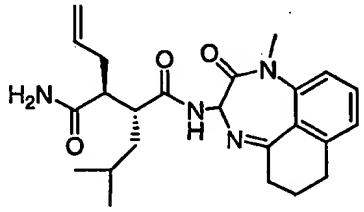
Example **1a'**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75-0.95 (m, 9H), 1.08-1.60 (m, br, 6H), 1.65-1.80 (m, 1H), 1.90-2.02 (m, 1H), 2.15-2.35 (m, 2H), 2.45-2.65 (m, 2H), 2.70-3.10 (m, br, 5H), 3.58-3.70 (m, 1H), 4.20-4.30 (m, 1H), 5.08 (d, J = 10 Hz, 1H), 5.14 (d, J = 17 Hz, 1H), 5.32 (s, br, 1H), 5.40 (d, J = 7 Hz, 1H), 5.78-5.85 (m, 1H), 7.15 (d, J = 8

Hz, 1H), 7.24-7.26 (m, 1H), 7.39 (d, J = 8 Hz, 1H), 7.50-7.60 (m, 1H); MS m/z 467.5 (MH^+).

Example **1a''**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75-0.95 (m, 9H), 1.08-2.05 (m, 10H), 2.15-2.35 (m, 2H), 2.40-2.60 (m, 1H), 2.60-2.75 (m, 1H), 2.80-3.15 (m, 3H), 3.58-3.70 (m, 1H), 4.15-4.26 (m, 1H), 5.06 (d, J = 10 Hz, 1H), 5.13 (d, J = 15 Hz, 1H), 5.32-5.42 (m, br, 2H), 5.78-5.85 (m, 1H), 7.15 (d, J = 7 Hz, 1H), 7.24-7.26 (m, 2H), 7.50-7.60 (m, 1H); MS m/z 467.5 (MH^+).

Example 1b

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-methyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide (Example **1b**)

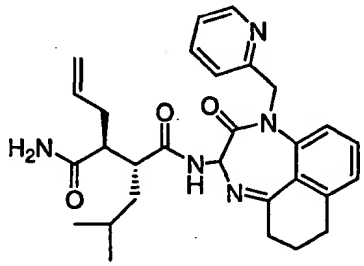


Ex. 1b

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-methyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide (**1b**) was prepared in the similar manner by alkylation of **1-12** with iodomethane. MS m/z 425.5 (MH^+).

Example 1c

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-(pyrid-2-ylmethyl)-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide (Example **1c**)

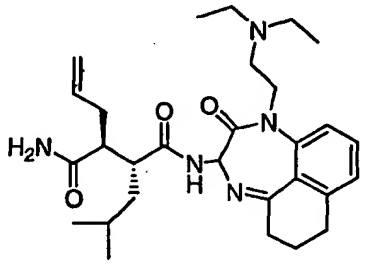


Ex. 1c

(2R, 3S)-3-allyl-2-isobutyl-N^1-(3-oxo-4-(2-pyridinylmethyl)-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide (Example 1c) was prepared in the similar manner by alkylation of **1-12** with 2-(bromomethyl)pyridine. MS *m/z* 502.5 (MH^+).

Example 1d

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-(2-(diethylamino)ethyl)-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide (Example **1d**)



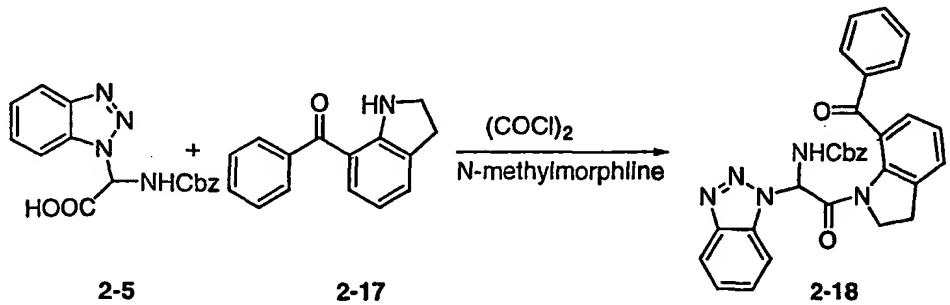
Ex. 1d

(2R, 3S)-3-allyl-2-isobutyl-N^1-{4-[2-(diethylaminoethyl)]-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl}-3-isobutylbutanediamide (**1d**) was prepared in the similar manner by alkylation of **1-12** with 2-bromo-N,N-diethylethylamine. MS *m/z* 510.5 (MH^+).

Example 2

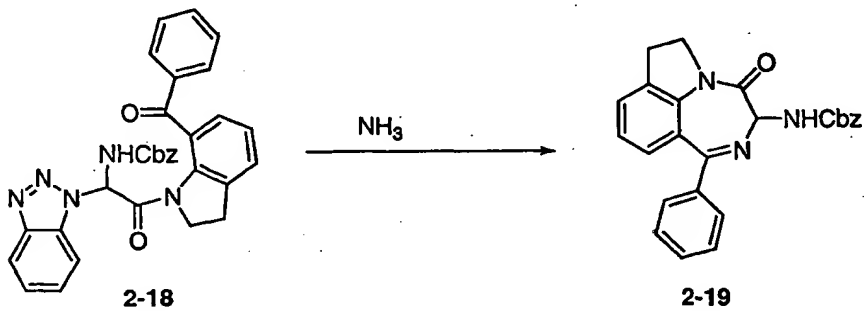
Representative procedure for 4-oxo-1-phenyl-3,4,6,7-tetrahydro[1,4]diazepino[6,7,1-hi]indole core **2.**

2,3-Dihydro-1H-indol-7-ylphenyl)methanone (**2-17**) was prepared according to the procedure of Y. Satoh et al Chem. Pharm. Bull. 1994, 42, 2071.



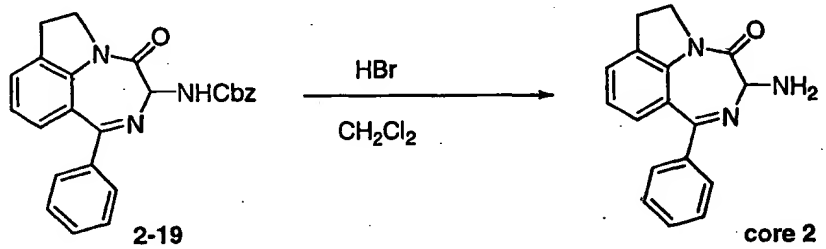
2-5 **2-17** **2-18**

To a solution of 2-(benzotriazol-1-yl)-N-(benzoloxycarbonyl)glycine (**2-5**, 28.1 g, 86.0 mmol) in anhydrous THF (200 mL) at 0°C was added oxalyl chloride (7.4 mL, 86 mmol) via syringe over 5 min., followed by addition of anhydrous DMF (1 mL). Stirring was continued for 3 h at 0°C. A solution of **2-17** (17.50 g, 78 mmol) and *N*-methylmorpholine (18.96 mL, 172 mmol) in anhydrous THF (120 mL) was added over *ca.* 30 min. The reaction mixture was slowly warmed to room temperature and stirred overnight. The precipitate was filtered and washed with cold THF. The mother liquor was evaporated, and the residue was purified on silica gel (50% ethyl acetate/hexane) to give **2-18** (7.5 g, 18%) as a yellow solid. MS *m/z* 554.4 $(M+Na)^+$, 530.4 $(M-H)^+$



2-18 **2-19**

2-18 (7.7 g, 14.5 mmol) was dissolved in THF (100 mL) and methanol (30 mL). The mixture was bubbled with anhydrous ammonia for 4 h and stirred overnight. The reaction mixture was concentrated and purified on silica gel (10% ethyl acetate/hexane) to give **2-19** (1.41 g, 24%). MS *m/z* 412.4 $(M+H)^+$, 434.4 $(M+Na)^+$, 410.4 $(M-H)^+$.

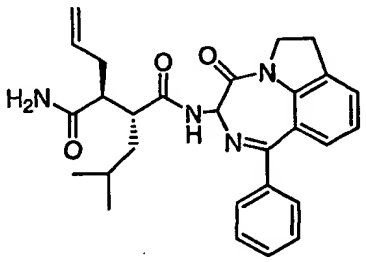


2-19 **core 2**

A solution of **2-19** (1.40 g, 3.4 mmol) in CH_2Cl_2 (5 mL) was saturated with anhydrous HBr gas for 2 h. The reaction mixture was then diluted with ether, and the precipitate was washed with ether by decantation. To the solid was added saturated aqueous Na_2CO_3 until pH>10. The aqueous layer was extracted with EtOAc. The organic extracts were combined, washed with brine, and dried (Na_2SO4). Evaporation of the solvent provided **core 2** (270 mg, 29%) as a yellow oil. MS *m/z* 278.3 $(M+H)^+$, 276.3 $(M-H)^+$.

Example 2a

(2R,3S)-3-allyl-2-isobutyl-N^1-(4-oxo-1-phenyl-3,4,6,7-tetrahydro[1,4]diazepino[6,7,1-hi]indol-3-yl)butandiamide (Example 2a)

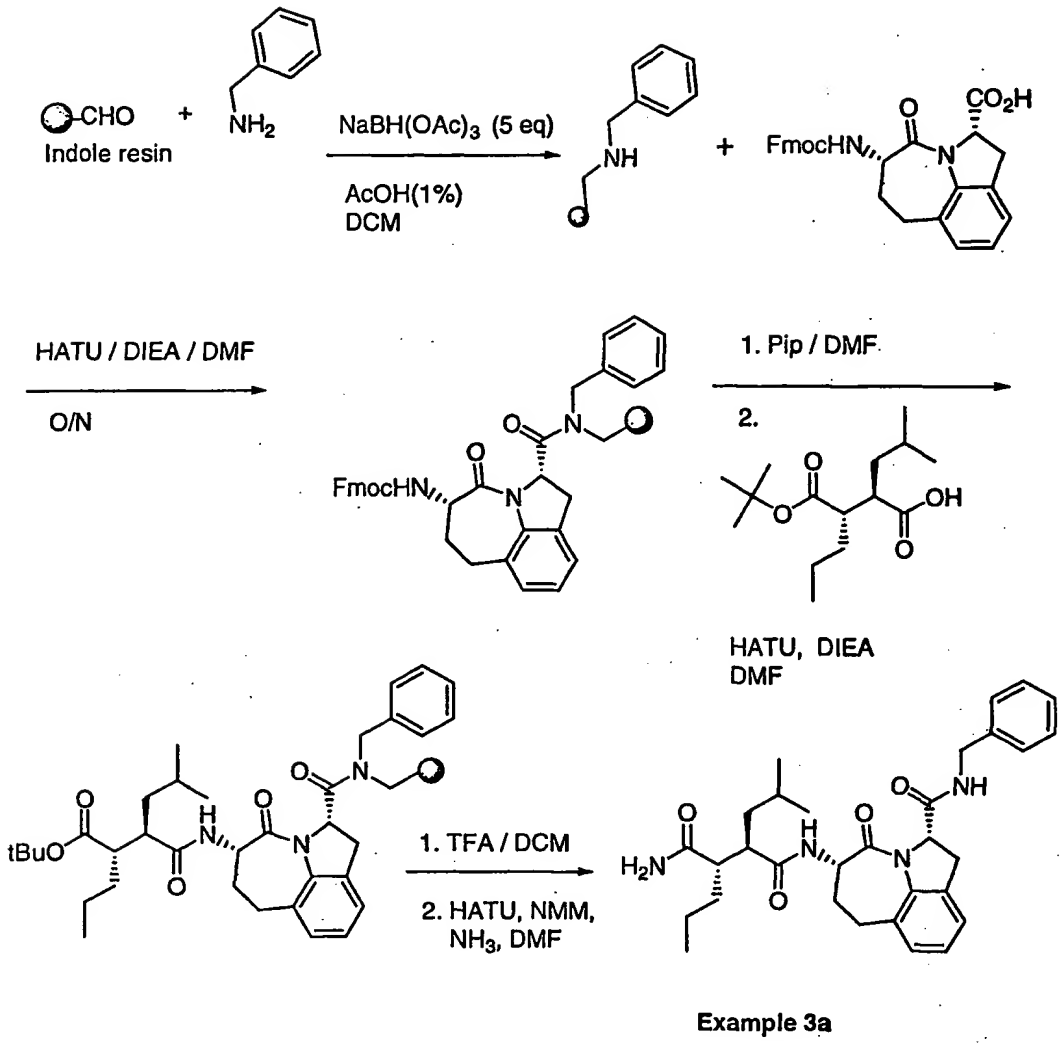


Ex. 2a

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-oxo-1-phenyl-3,4,6,7-tetrahydro[1,4]diazepino[6,7,1-hi]indol-3-yl)butandiamide (Ex. **2a**) can be prepared from core **2** and **1-10** as illustrated in the synthesis of **1-12**.

Example 3

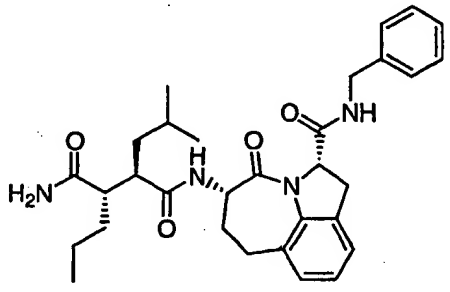
Representative procedure for 4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indole core.



Example 3a

Example 3a.

N1-(2-Benzylcarbamoyl-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-2-isobutyl-3-propyl-succinamide.



A portion of (3-formylindolyl)acetamidomethyl polystyrene resin (0.100 g, 0.75 mmol / g, 0.075 mmol, Novabiochem, Inc.) was washed and suspended in about 2 mL CH_2Cl_2. Then 5 eq (0.375 mmoles, M.W. = 107.16, d=0.781, 51.5 μL) of benzylamine was added followed by 5 eq (0.375 mmoles, M.W.= 212, 80 mg) of $NaBH(OAc)_3$ and 1% AcOH (v/v, 20 μL) and the reaction suspension was allowed to shake overnight. Next day, a small sample was checked with Chloranil test (positive).

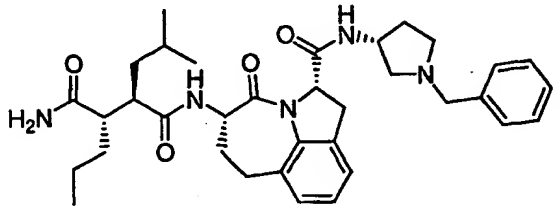
The resin was washed thoroughly with CH_2Cl_2, MeOH, DMF and suspended in DMF. Then 5 eq (0.375 mmoles, M.W. = 468.5, 176 mg) of Fmoc-Haic (Neosystems, Inc., or see Tetrahedron Letters, **1994**, *35*, (41), 7513-7516) was added followed by 5 eq (0.375 mmoles, M.W. = 380.2, 143 mg) of HATU and 10 eq (0.75 mmoles, M.W. = 129.25, d = 0.742, 131 μL) of DIEA. The reaction suspension was allowed to shake overnight. Next day, a small sample was monitored by Chloranil test (negative).

The resin was washed thoroughly with DMF, MeOH, CH_2Cl_2, DMF and the Fmoc group was deprotected with 50% Piperidine / DMF for 10 min and the resin was washed again as above. Then 50 mg of resin was taken and suspended in DMF and coupled with 5 eq (0.19 mmoles, M.W. = 272.4, 52 mg) of Succinic acid **10** (Scheme 2) followed by 5 eq (0.19 mmoles, M.W. = 380.2, 72 mg) of HATU and 10 eq (0.38 mmoles, M.W. = 129.25, d = 0.742, 66 μL) of DIEA was added and the resin was allowed to shake overnight. Next day, a small sample was monitored by Ninhydrin test (negative).

The resin was washed thoroughly with DMF, MeOH and CH_2Cl_2 and dried well under vacuum. The resin was treated with a mixture of TFA/ CH_2Cl_2(9:1) for 3 h, filtered and concentrated in vacuum and azeotroped with dichloromethane and hexane to remove the residual TFA. The residue was triturated with Ether/hexane mixture to give the carboxylic acid. The acid (0.034 g, 0.064 mmol) was dissolved in 1 ml of DMF and HATU (0.032 g, 0.032 mmol) and 4-Methylmorpholine were added and stirred for 15 min. Then NH_3 (g) was bubbled for a min. and stirred for 2 h. The reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with satd. brine soln., dried over anhydrous Na_2SO_4, evaporated under high vacuum and dried under vacuum to give the crude amide. Purification by reverse phase HPLC provided the title compound of Example 3a as a white powder (12 mg). MS $(M+H)^+$ = 533.5.

Example 3b.

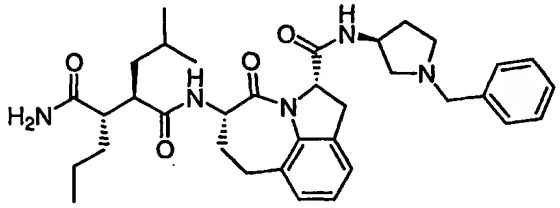
N1-[2-(1-Benzyl-pyrrolidin-3-ylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide.



The compound of Example 3b was synthesized in a manner similar to the synthesis of the compound of Example 3a, but using (R)-3-amino-1-benzylpyrrolidine as the amine in the last step. Cleavage of 100 mg of functionalized resin (0.52 mmol/g) and purification by RP-HPLC provided 10.5 mg (30%) of the title compound as a white powder. MS $(M+H)^+ = 602.5$.

Example 3c.

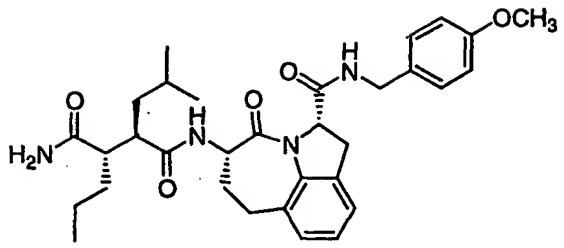
N1-[2-(1-Benzyl-pyrrolidin-3-ylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide.



The compound of Example 3c was synthesized in a manner similar to the synthesis of the compound of Example 3a, but using (S)-3-amino1-benzylpyrrolidine as the amine in the last step. Cleavage of 100 mg of functionalized resin (0.52 mmol/g) and purification by RP-HPLC provided 7.0 mg (22%) of the title compound as a white powder. MS $(M+H)^+ = 602.5$.

Example 3d.

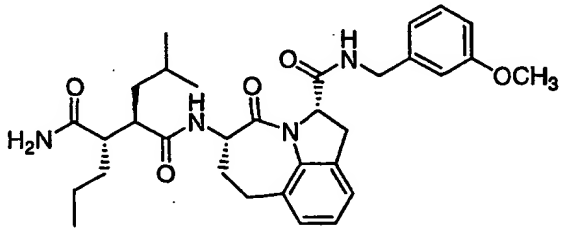
2-Isobutyl-N1-[2-(4-methoxy-benzylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-3-propyl-succinamide.



The compound of Example 3d was synthesized in a manner similar to the synthesis of the compound of Example 3a, but using 4-methoxybenzylamine as the amine in the last step. Cleavage of 100 mg of functionalized resin (0.53 mmol/g) and purification by RP-HPLC provided 12.0 mg (40%) of the title compound as a white powder. MS $(M+H)^+ = 563.43$.

Example 3e.

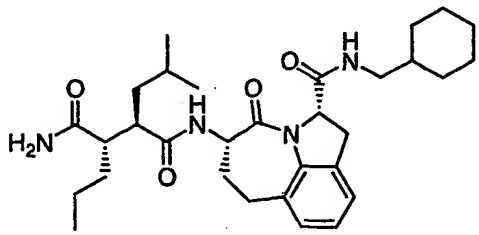
2-Isobutyl-N1-[2-(3-methoxy-benzylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-3-propyl-succinamide.



The compound of Example 3e was synthesized in a manner similar to the synthesis of the compound of Example 3a, but using 3-methoxybenzylamine as the amine in the last step. Cleavage of 100 mg of functionalized resin (0.53 mmol/g) and purification by RP-HPLC provided 17.0 mg (56%) of the title compound as a white powder. MS $(M+H)^+ = 563.43$.

Example 3f.

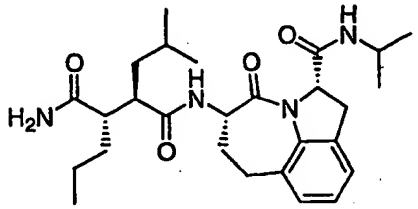
N1-[2-(Cyclohexylmethyl-carbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide.



The compound of Example 3f was synthesized in a manner similar to the synthesis of the compound of Example 3a, but using cyclohexylmethylamine as the amine in the last step. Cleavage of 100 mg of functionalized resin (0.53 mmol/g) and purification by RP-HPLC provided 9.0 mg (32%) of the title compound as a white powder. MS $(M+H)^+ = 539.5$.

Example 3g.

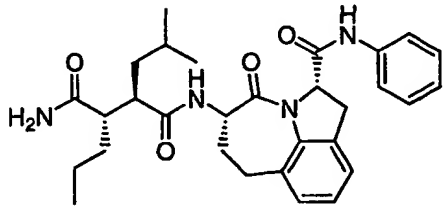
2-Isobutyl-N1-(2-isopropylcarbamoyl-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-3-propyl-succinamide.



The compound of Example 3g was synthesized in a manner similar to the synthesis of the compound of Example 3a, but using isopropylamine as the amine in the last step. Cleavage of 100 mg of functionalized resin (0.55 mmol/g) and purification by RP-HPLC provided 15.5 mg (60%) of the title compound as a white powder. MS $(M+H)^+ = 485.5$.

Example 3h.

2-Isobutyl-N1-(4-oxo-2-phenylcarbamoyl-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-3-propyl-succinamide.

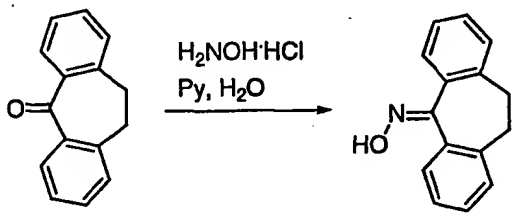


The compound of Example 3h was synthesized in a manner similar to the synthesis of the compound of Example 3a, but using aniline as the amine in the last step. Cleavage of 50 mg of functionalized resin (0.54 mmol/g) and purification by RP-HPLC provided 4.0 mg (38%) of the title compound as a white powder. MS $(M+H)^+ = 519.4$.

Example 4.

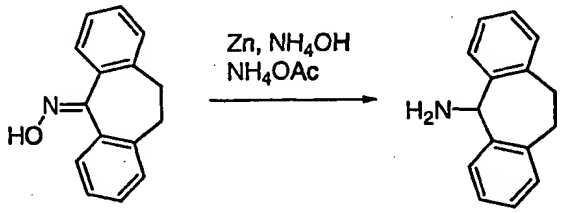
tert-Butyl 2-isobutyl-N1-(10,11-dihydro-5H-dibenzo[a,d]cycloheptene-5-yl)-3-allyl-succinate or 2-Isobutyl-N1-(dibenzosuberan-5-yl)-3-allyl-succinate tert-butyl ester.

Compound **4-3** was made according to P. Melloni et al *J. Med. Chem.* **1979**, 22(2), 183-191.



4-1 **4-2**

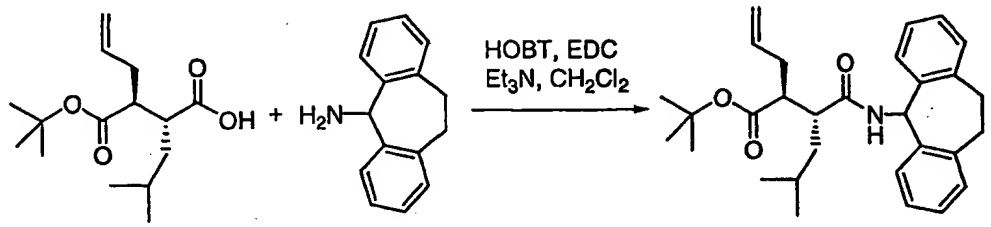
A mixture of hydroxylamine hydrochloride (8.35 g, 120 mmol) and dibenzosuberone (**4-1**, 10 g, 48 mmol) in pyridine (30 mL) and H_2O (30 mL) was refluxed for 3 days. Pyridine was removed from the reaction mixture *in vacuo*. The residue was extracted with ethyl acetate. The organic extracts were combined and washed with water, brine, and dried (Na_2SO_4). The solvent was evaporated, and the residue was crystallized from ethyl acetate and hexane to give **4-2** (2.95 g, 28%) as a white crystalline. MS *m/z* 224.1 (MH^+).



4-2 **4-3**

To a solution of **4-2** (2.95 g, 13 mmol) in ethanol (20 mL) and DMF (3 mL) was added zinc powder (4.2 g, 6.5 mmol), ammonium acetate (0.5 g, 6.5 mmol), and ammonium hydroxide (65 mL) sequentially. The reaction mixture was refluxed for 3 h, and then cooled to room temperature. After diluted with ether (100 mL), the reaction mixture was made basic (pH>10) with 35% NaOH, and extracted with ether. The organic extracts were combined, washed with water, brine, and dried (K_2CO_3). Evaporation of the solvent provided **4-3** (2.27 g, 83%) as a white solid. ^1H NMR (300

MHz, $CDCl_3$) δ 7.10 – 7.50 (m, 8 H), 5.47 (s, 1 H), 3.30 – 3.50 (m, 2 H), 3.10 – 3.25 (m, 2 H), 2.53 (br s, 2 H).



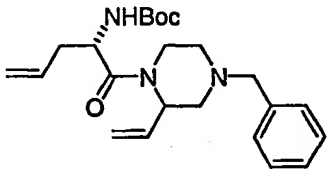
4-4 4-3 Example 4

Compound **4-4** (135 mg, 0.500 mmol), **4-3** (105 mg, 0.500 mmol) and 1-hydroxybenzotriazole hydrate (HOBT, 81 mg, 0.60 mmol) were suspended in CH_2Cl_2, and cooled to 0 °C. To this mixture 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl, 192 mg, 1.00 mmol) and triethylamine (0.10 mL, 0.75 mmol) were added. After being stirred for 20 h at ambient temperature, the reaction mixture was diluted with ethyl acetate. The organic layer was washed with water, brine and dried (Na_2SO_4). After evaporation of the solvent, the solid obtained was recrystallized from ethyl acetate and hexane to afford Example **4** (200 mg, 87%). MS *m/z* 462.3 (MH^+).

Example 5.

(2*R*,3*S*)-3-Allyl-*N*^{1}-[(7*S*)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-yl]-2-isobutylbutanediamide.

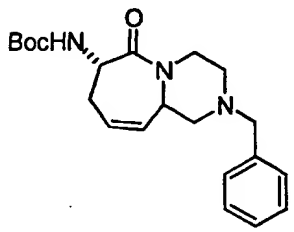
Preparation of *tert*-butyl (1*S*)-1-[(4-benzyl-2-vinyl-1-piperazinyl)carbonyl]-3-butenylcarbamate.



(2*S*)-2-[(*tert*-butoxycarbonyl)amino]-4-pentenoic acid (466 mg, 2.17 mmol) and 1-benzyl-3-vinylpiperazine (436 mg, 2.17 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (HOBT, 622 mg, 3.26 mmol) were combined with anhydrous CH_2Cl_2 (10 mL) at room temperature. Et_3N (0.74 mL, 5.43 mmol) was added

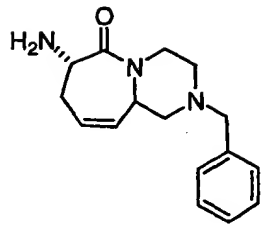
in one portion. The resulted solution was maintained at room temperature for 18 h at which time it was concentrated in vacuo to a volume of approximately 5 mL. Then the solution was purified by silica gel chromatography (SGC) eluting with 2:1 hex-EtOAc. The title compound (a pair of diastereomers) was obtained (171 mg, 20%) as a pale-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (s, 5H), 5.99-5.82 (m, 1H), 5.81-5.65 (m, 1H), 5.50-5.00 (m, 6H), 4.75-4.23 (m, 2H), 3.70-3.37 (m, 3H), 3.11-2.79 (m, 2H), 2.59-2.00 (m, 4H), 1.42 (s, 9H) ppm. MS (CI) 400.6 (M+H).

Preparation of *tert*-butyl (7*S*)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-ylcarbamate.



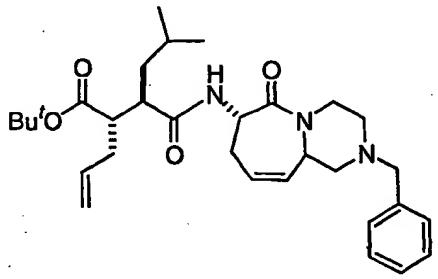
tert-Butyl (1*S*)-1-[(4-benzyl-2-vinyl-1-piperazinyl)carbonyl]-3-butenylcarbamate (250 mg, 0.63 mmol) and Grubb's catalyst (26 mg, 0.03 mmol) were combined in toluene (32 mL) at room temperature. This mixture was degassed via vacuum-argon three times at room temperature. Then CH_2Cl_2 (32 mL) was added in one portion. The reaction mixture was heated at reflux for 5 days, then concentrated *in vacuo*. The residue was purified by SGC (4:1 hex-EtOAc) to give the title product (103 mg, 44%) as a yellow powder. The ^{1}H NMR spectrum was consistent with the presence of one diastereomer, not assigned. (300 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.76-5.72 (m, 2H), 5.67-5.58 (m, 1H), 5.35-5.01 (m, 1H), 4.68 (br s, 1H), 4.00 (m, 1H), 3.64 (d, 1H, J = 13.1 Hz), 3.42 (d, 1H, J = 13.2 Hz), 3.09 (dt, 1H, J = 13.5, 4.1 Hz), 2.91-2.86 (m, 1H), 2.76-2.72 (m, 2H), 2.26-2.00 (m, 3H), 1.44 (s, 9H) ppm.

Preparation of (7*S*)-7-Amino-2-benzyl-1,3,4,7,8,10a-hexahydropyrazino[1,2-a]azepin-6(2*H*)-one.



tert-Butyl (7*S*)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-ylcarbamate (140 mg, 0.38 mmol) was dissolved in 4 mL CH_2Cl_2 at room temperature. Trifluoroacetic acid (TFA, 2 mL) was added in 3 portions. The reaction mixture was maintained at room temperature for 18 h at which time it was concentrated *in vacuo* to give the bis-TFA salt (103 mg, 100%) of the title compound as a brown heavy oil. Part of this crude sample (73 mg, 0.15 mmol) was suspended in 5 mL of $CHCl_3$ at room temperature. A saturated aqueous solution of K_2CO_3 (5 mL) was added in one portion. The two-phase mixture was stirred vigorously at room temperature for 2 h, then diluted with 20 mL of H_2O. The resulting mixture was extracted with $CHCl_3$ (3 x 20 mL). The organic layers were combined and washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The title free amine was isolated (39 mg, 100%) as a tan colored powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35- 7.28 (m, 5H), 5.75-5.74 (m, 1H), 5.64-5.58 (m, 1H), 4.66 (br s, 1H), 4.45 (dd, 1H, J = 12.8, 5.8 Hz), 4.00 (dt, 1H, J = 13.5, 10.9, 1.1 Hz), 3.64 (d, 1H, J = 13.2 Hz), 3.43 (d, 1H, J = 13.2 Hz), 3.09 (dt, 1H, J = 13.5, 4.1 Hz), 2.91-2.88 (m, 1H), 2.79-2.72 (m, 1H), 2.61-2.52 (m, 1H), 2.28- 1.90 (m, 5H) ppm.

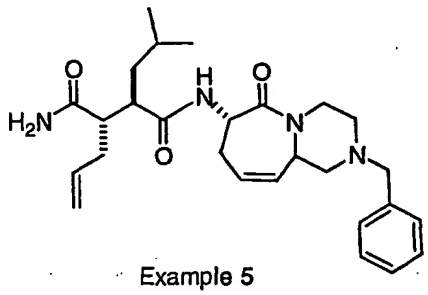
Preparation of *tert*-butyl (2*S*)-2-[(1S)-1-({[(7*S*)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-yl]amino}carbonyl)-3-methylbutyl]-4-pentenoate.



(7*S*)-7-Amino-2-benzyl-1,3,4,7,8,10a-hexahydropyrazino[1,2-a]azepin-6(2*H*)-one bis-trifluoroacetic acid salt (73 mg, 0.27 mmol), succinate **1-10** (90 mg, 0.32 mmol), and HATU (133 mg, 0.35 mmol) were combined with 1 mL of DMF at room

temperature. This solution was stirred at room temperature for 5 min at which time diisopropylethyl amine (55 mg, 0.43 mmol) was added in one portion. The reaction was maintained at room temperature for 18 h and concentrated *in vacuo* at 60 °C. The residue was purified by SGC (4:1 hex-EtOAc) to provide the title compound (101 mg, 71%) as a pale-yellow heavy oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 6.94 (d, 1H, J = 6.9 Hz), 5.80-5.45 (m, 4H), 5.05-4.98 (m, 2H), 4.69 (br s, 1H), 4.07-3.99 (m, 1H), 3.64 (d, 1H, J = 13.1 Hz), 3.44 (d, 1H, J = 13.1 Hz), 3.11 (dt, 1H, J = 13.4, 4.0 Hz), 2.95-2.72 (m, 2H), 2.60-2.38 (m, 2H), 2.30-2.14 (m, 4H), 2.12-1.96 (m, 1H), 1.79-1.50 (m, 3H), 1.44 (s, 9H), 1.15-1.00 (m, 1H), 0.91-0.84(m, 6H) ppm.

Preparation of (2*R*,3*S*)-3-allyl-*N*^{1}-[(7*S*)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-yl]-2-isobutylbutanediamide (Example 5).



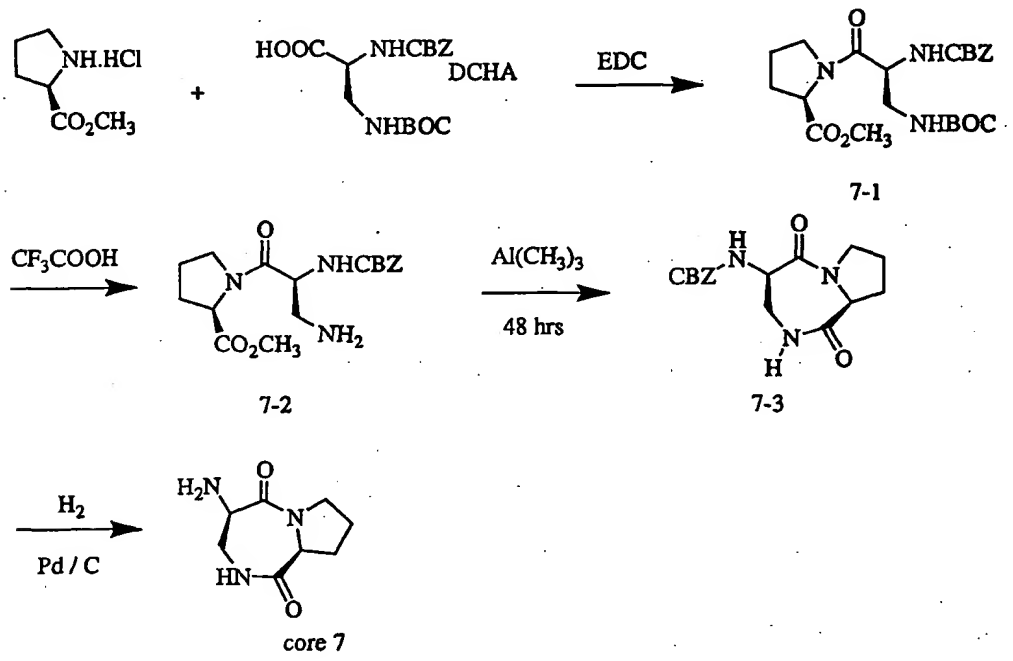
Example 5

tert-Butyl (2*S*)-2-[(1S)-1-({[(7S)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-yl]amino}carbonyl)-3-methylbutyl]-4-pentenoate (90 mg, 0.17 mmo) was dissolved in 2 mL of CH_2Cl_2 at room temperature. With stirring 1 mL of TFA was added in three portions. The solution was maintained at room temperature for 18 h, then concentrated *in vacuo*. The residue was combined with HATU (109 mg, 1.08 mmol), diisopropylethyl amine (109 mg, 0.84 mmol) and 1 mL of DMF. To this solution at room temperature was intoduced a stream of ammonia for 4 min. Additional 1 mL of DMF was added, and the mixture was was heated at 100 °C until the precipitate dissolved. This solution was then maintained at room temperature for 18 h at which time it was concentrated in vacuo at 60 °C. The residue was purified by SGC (79:1 CH_2Cl_2-MeOH) to give the title compound (50 mg, 63%) as a tan colored foam. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 7.11 (d, 1H, J = 6.6 Hz), 6.11 (br s, 1H), 5.79-5.44 (m, 5H), 5.10-5.02 (m, 2H), 4.70 (br s, 1H), 4.20-3.99 (m, 1H), 3.64

(d, 1H, J = 13.2 Hz), 3.44 (d, 1H, J = 13.2 Hz), 3.10 (dt, 1H, J = 13.5, 4.1 Hz), 2.95-2.72 (m, 3H), 2.60-2.45 (m, 2H), 2.40-1.99 (m, 5H), 1.72-1.16 (m, 3H), 0.90-0.85 (m, 6H) ppm.

Example 7.

Representative preparation for 4-amino-hexahydro-pyrrolo[1,2-a][1,4]diazepine-1,5-dione core **7**.



To a solution of N-α-Cbz-N-β-Boc-l-diaminopropionic acid dicyclohexylamine salt (14g, 26.9mmol) in 300ml CH_2Cl_2 was added D-proline methylester HCl (5.0g, 31.2mmol), followed by 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl (EDC, 8.0g, 41.7mmol, 1.5 eq.), 1-hydroxybenzotriazole hydrate (HOBT, 7.5g, 55.5mmol, 2.0eq.) and triethylamine (10ml, 72mmol, 2.6 eq.). The mixture was stirred overnight. The solvents were removed under reduced pressure to give a white solid, which was taken up in EtOAc and water. The organic layer was washed with water, brine and dried over Na_2SO_4. The solution was concentrated to give the crude product as a solid, which was purified by column chromatography on silica gel using EtOAc:hexane (7:3) to give **7-1** as a white solid (12.1g, 100%). MS: ^{1}HNMR(300 MHz, $CDCl_3$) 1.4 (s, 9H), 1.9-2.3

(m, 3H), 3.3-3.5 (m, 2H), 3.7 (s, 3H), 3.7-3.9 (m, 1H), 4.4 (m, 1H), 4.6-4.7 (m, 1H), 5.0-5.2 (m, 3H), 5.8-6.0 (m, 1H), 7.2-7.4 (m, 5H). MS: 450.2 (M+H), 472.3 (M+Na).

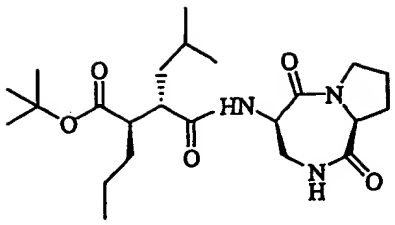
Compound **7-1** (3.5g, 7.8mmol) was dissolved in 100ml of 50% trifluoroacetic acid (TFA) in CH_2Cl_2 and stirred at ambient temperature for one hour. The solvents were then removed under reduced pressure and the resulting oil was redissolved in 30ml of toluene and reconcentrated to remove residual TFA. The product (**7-2**) was obtained as a slightly yellow solid **7-2** (2.5g, 92%). ^{1}HNMR (300MHz, $CDCl_3$) 1.8-2.0 (m, 2H), 2.0-2.2 (m, 1H), 3.2-3.8 (m, 6H), 4.3-4.9 (m, 3H), 4.9-5.1 (m, 3H), 7.2-7.4 (m, 5H). MS: 350.3 (M+H), 372.2 (M+Na).

Trimethylaluminum (22mmol, 1.0M in hexane) was added to a solution of **7-2** (2.5g, 7.2mmol) in 50ml 1,2-dichloroethane at room temperature and the reaction mixture was heated to 75 °C for 48 hours. The reaction was quenched with water and then enough 1.0 N HCl solution was added to the mixture to give a clear solution. The aqueous solution was extracted with $CHCl_3$ (2x200ml). The combined organic layers were dried with brine and Na_2SO_4. Evaporation of the organic solvent gave a sticky oil which was purified by column chromatography on silica gel with 100% EtOAc to give a white solid (**7-3**, 800mg, 35%). ^{1}HNMR (300 MHz, $CDCl_3$) 1.7-1.9 (m, 2H), 2.0-2.2 (m, 1H), 2.6-2.8 (m, 1H), 3.2-3.4 (m, 1H), 3.4-3.7 (m, 3H), 4.4-4.6 (m, 1H), 4.8-5.0 (m, 1H), 5.0-5.2 (m, 2H), 6.2 (m, 1H), 6.4-6.5 (s, 1H), 7.2-7.4 (m, 5H). MS: 318.2 (M+H).

A solution of **7-3** (4.0g, 12.6mmol) in 100ml EtOAc was shaken with 1.0g Pd/C (5% on activated carbon) under H_2 (~50psi) for 2hrs. The reaction mixture was filtered and the solvent was removed under reduced pressure to give a white solid **7** (1.8g, 9.8mmol, 78%). MS: 184.3 (M+H).

Example 7a.

3-(1,5-Dioxo-octahydro-pyrrolo[1,2-a][1,4]diazepin-4-ylcarbamoyl)-5-methyl-2-propyl-hexanoic acid tert-butyl ester.

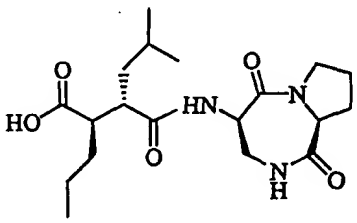


Example **7a**

To a solution of core **7** (350mg, 1.9mmol) in 20ml DMF at room temperature was added propyl-succinate X (510mg, 1.9mmol), o-(7-azabenzotriazol-1-yl)-N,N,N,N,-tetramethyluronium hexafluorophosphate (HATU, 900mg, 2.4mmol) and then diisopropylethylamine (DIPEA, 0.4ml, 2.3mmol). The mixture was stirred at room temperature overnight. The reaction was quenched with 10ml water. The solvents were removed under reduced pressure to give a viscous oil which was taken up in EtOAc and water (1:1). The organic layer was washed with water, brine and Na_2SO_4. The solvents were evaporated under reduced pressure to give an oily crude product which was purified by column chromatography in 5% methanol/CH_2Cl_2 to give Example **7a** as a white solid (230mg, 0.53mmol, 28%). MS: 438.4 (M+H).

Example 7b.

3-(1,5-Dioxo-octahydro-pyrrolo[1,2-a][1,4]diazepin-4-ylcarbamoyl)-5-methyl-2-propyl-hexanoic acid.

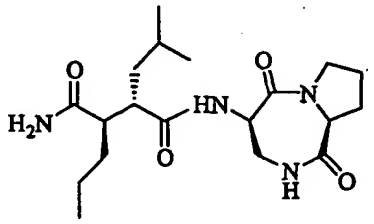


Example **7b**

Example **7a** (230mg, 0.53mmol) was dissolved in 20ml of 50% TFA in CH_2Cl_2 and stirred at room temperature for 2hrs. The solvents were removed under reduced pressure and the resulting oil was taken up in 20ml toluene and concentrated to give Example **7b** as a slightly yellow solid (190mg, 0.50mmol). MS: 380.2 (M-H).

Example 7c.

N1-(1,5-Dioxo-octahydro-pyrrolo[1,2-a][1,4]diazepin-4-yl)-2-isobutyl-3-propyl-succinamide.

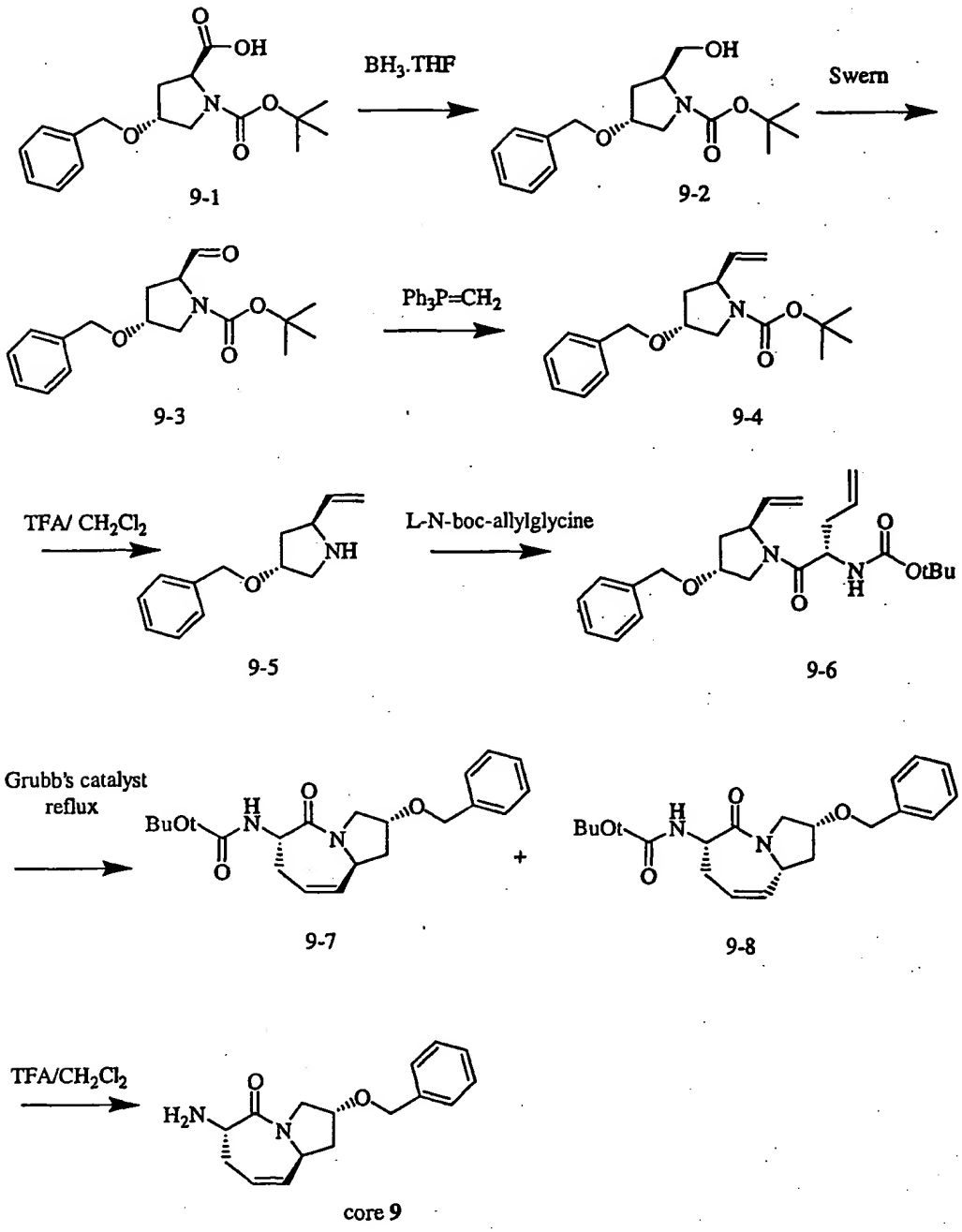


Example **7c**

To a solution of Example **7b** (190mg, 0.50mmol) in 20ml DMF was added HATU (250mg, 0.56mmol), followed by DIPEA (0.3ml, 1.7mmol). After the reaction mixture was treated with ammonia gas for 5 minutes, the reaction was stirred at room temperature overnight. After quenching the reaction was with 10ml water, the solvents were removed under reduced pressure and the resulting oil was taken into EtOAc and water (1:1). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of solvents and purification by column chromatography on silica gel with 10% methanol in CH_2Cl_2 provided Example **7c** as a white solid (3mg, 0.008mmol, 1.6%). ^{1}HNMR (300MHz, CD_3OD) 0.8-1.0 (m, 9H), 1.0-1.7 (m, 7H), 1.8-2.1 (m, 3H), 2.2-2.5 (m, 3H), 3.2 (m, 1H), 3.4-3.8 (m, 5H), 3.9-4.0 (m, 1H), 4.2-4.3 (m, 1H). MS: 381.2 (M+H), 403.2 (M+Na).

Example 9.

Representative preparation for the 1,2,3,6,7,9a-hexahydro-pyrrolo[1,2-a]azepin-5-one core **9**.



A solution of **9-1** (17.0g, 53mmol) in 100ml THF was added to a solution of BH_3-THF (100ml, 100mmol) over a period of 30 minutes under nitrogen at 0 °C. After the mixture was stirred for an additional one hour at 0 °C, the reaction was quenched with 25ml of 10% HOAc in methanol solution, and the solvents were evaporated under reduced pressure to give a viscous oil. The crude product was taken up in EtOAc, washed with 1.0N HCl, water and saturated $NaHCO_3$, and then dried over brine and

Na_2SO_4. Evaporation of solvents provided a colorless oil **9-2** (16.5g, 100%) which was directly used in the next step without purification. ^{1}HNMR (300 MHz, $CDCl_3$) 1.48 (s, 9H), 1.6-1.8(m, 1H), 2.1-2.3(m, 1H), 3.3-3.5 (m, 1H), 3.5-3.8 (m, 3H), 4.0-4.2 (m, 2H), 4.4-4.6 (m, 2H), 5.0 (m, 1H), 7.2-7.4 (m, 5H). MS: 308.2 (M+H), 371.2 (M+Na+CH3CN), 637.3 (2M+Na).

In a 1000ml three-neck flask, a solution of oxalyl chloride (11.0g, 86.7mmol) in 50ml CH_2Cl_2 was cooled in dry-ice bath. To this solution, a solution of DMSO (12ml, 170 mmol) in 100ml CH_2Cl_2 was added slowly. After 10 minutes, the solution of **9-2** (16.3g, 53mmol) in 200ml CH_2Cl_2 was added into the above solution dropwise over 10 minutes. After the reaction mixture was stirred in a dry-ice bath for additional 30 minutes, N-methylmorpholine (34.3g, 339mmol) was added. The reaction was stirred for another 10 minutes in a dry-ice bath before warming to zero degrees in an ice bath. After 20 minutes, the yellow slurry solution was poured into ice water. The aqueous solution was extracted with CH_2Cl_2 (2x200ml). The combined organic extracts were washed with 1.0N NaOH (3x100ml), and then saturated $NaHCO_3$ (2x100ml). The solution was dried with brine and Na_2SO_4. Concentration provided **9-3** as a yellow oil, which was used directly in the next step without purification. ^{1}HNMR (300 MHz, $CDCl_3$) 1.4-1.6(d, 9H), 1.9-2.0 (m, 1H), 2.2-2.4 (m, 1H), 3.4-3.8 (m, 2H), 4.0-4.4(m, 2H), 4.4-4.6 (m, 2H), 7.2-7.4 (m, 5H), 9.4-9.6 (m, 1H).

A solution of sodium bis(trimethylsilyl)amide (12.0g, 62.2mmol) in 200ml THF was added into a suspension of methyltriphenylphosphonium bromide (22.8g, 63.8mmol) in 200ml THF at zero degree over 30 minutes to give a yellow slurry which was stirred at zero degree for additional 30 minutes. A solution of **9-3** in 100ml THF was added to the slurry above over a period of 30 minutes. After addition, the reaction was complete in 10 minutes (TLC). The reaction mixture was poured into ice water and the aqueous layer was adjusted to pH 7 with 1.0 N HCl. The mixture was extracted with 3 x 100 mL EtOAc. The combined organic layers were washed with saturated $NaHCO_3$ and brine, then dried over Na2SO4. The organic solvent was evaporated under reduced pressure to give the crude product as an oil, which was purified by column chromatography on silica gel in 10% EtOAc/hexane to give **9-4** as a slightly yellow oil (12g, 39.6mmol, 75%). ^{1}HNMR (300MHZ, $CDCl_3$) 1.4 (s, 9H), 1.8-2.0 (m, 1H), 2.2-2.3

(m, 1H), 3.4-3.8 (m, 2H), 4.0-4.6 (m, 4H), 5.0-5.2 (m, 2H), 5.6-5.8 (m, 1H), 7.2-7.4 (m, 5H). MS: 326.2 (M+H), 367.2 (M+Na+CH3CN).

A solution of **9-4** in 100ml of 50% TFA in CH_2Cl_2 was stirred at room temperature for 2hrs. The solvents were removed under reduced pressure and the resulting oil was redissolved in 50ml of toluene and concentrated to give **9-5** as a dark oil (8.0g, 39.4mmol, 100%). ^{1}HNMR (300 MHz, $CDCl_3$) 1.9-2.1 (m, 1H), 2.3-2.4 (m, 1H), 3.4-3.7 (m, 2H), 4.2-4.4 (m,2H), 4.4-4.6 (s, 2H), 5.4-5.6 (m, 2H), 5.8-6.0 (m, 1H), 7.2-7.4 (m, 5H). MS: 204.3 (M+H).

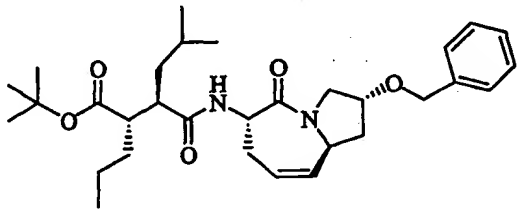
To a solution of **9-5** (8.0g, 39.4mmol) in 200ml CH_2Cl_2 was added L-N-boc-allylglycine (9.0g, 42mmol), EDC (12.0g, 62.2mmol), HOBT (8.0g, 59.2mmol) and triethylamine (8ml, 57.3mmol). The reaction mixture was stirred at ambient temperature overnight. The reaction mixture was concentrated to give a viscous oil which was taken up in EtOAc and water. The organic layer was washed with water, brine and dried over Na_2SO_4. The solvent was evaporated and the oily crude product was purified by column chromatography on silica gel in 20% EtOAc/hexane to give **9-6** as a colorless oil (10.0g, 25mmol, 60%). ^{1}HNMR (300 MHz, $CDCl_3$) 1.4 (s, 9H), 1.8-2.0 (m, 1H), 2.2-2.6 (m, 3H), 3.4-3.6 (m, 1H), 3.7-3.9 (m, 1H), 4.0-4.2 (m, 1H), 4.4-4.8 (m, 3H), 5.0-5.2 (m, 4H), 5.3-5.5 (m, 1H), 5.6-5.9 (m, 2H), 7.2-7.4 (m, 5H). MS: 401.2 (M+H), 423.2 (M+Na).

To a solution of **9-6** (10.0g, 25mmol) in 1000ml of 50% CH_2Cl_2 in toluene at 100 degree was added 1.0g, (1.2mmol) bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride (Grubb's catalyst). After an interval of 4 hours, an identical portion of catalyst was added. After an additional interval of 4 hours, an additional 500mg of catalyst was added prior to heating overnight. The reaction mixture was then cooled to room temperature and filtered through a layer of celite. The solvents were removed to give a dark oil. GC-MS analysis suggested the presence of approximately 5% of the epimer **9-8**. The crude oil was purified by column chromatography on silica gel in 5% methanol/ CH_2Cl_2, which provided the major product **9-7** (3.7g, 9.95mmol, 40%). ^{1}HNMR (300MHz, $CDCl_3$) 1.4 (s, 9H), 1.8-2.0 (m, 1H), 2.4-2.6 (m, 2H), 2.6-2.8 (m, 1H), 3.5-3.7 (m, 1H), 3.8-4.2 (m, 3H), 4.4-4.6 (m, 2H), 4.7-4.9(m, 1H), 5.6-5.8 (m, 2H), 7.2-7.4 (m, 5H). MS: 373.2 (M+H), 767.5 (2M+Na).

Compound **9-7** was dissolved in 100ml of 50% TFA in CH_2Cl_2 was stirred at room temperature for 2hrs. The solvents were removed under reduced pressure and the resulting oil was redissolved in 50ml of toluene and concentrated to give bicyclic core **9**. ^{1}HNMR (300 MHz, $CDCl_3$) 1.8-2.0 (m, 1H), 2.3-2.5 (m, 1H), 2.6-2.8 (m, 1H), 2.8-3.0 (m, 1H), 3.6-3.8 (m, 2H), 3.8-4.0 (m, 1H), 4.0-4.1 (m, 1H), 4.4-4.6 (m, 2H), 4.6-4.8 (m, 1H), 5.8-6.0 (m, 1H), 6.0-6.2 (m, 1H), 7.0-7.4 (m, 5H). MS: 273.3 (M+H).

Example 9a.

3-(2-Benzyloxy-5-oxo-2,3,5,6,7,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-6-ylcarbamoyl)-5-methyl-2-propyl-hexanoic acid tert-butyl ester.

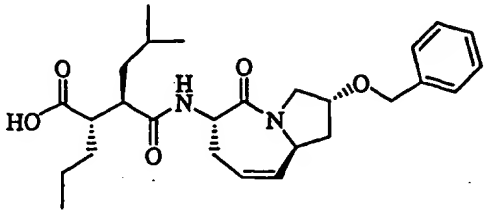


Example **9a**

To a solution of bicyclic core **9** (2.0g, 7.4mmol) in 50ml DMF was added the appropriate propyl-succinate t-butyl ester (2.0g, 7.4mmol), HATU(3.7g, 9.7mmol), and DIPEA (2.5ml, 14.3mmol). The reaction mixture was stirred at room temperature overnight, then quenched with 10ml water. The solvents were removed under reduced pressure to give a viscous oil which was taken into EtOAc and water. The organic layer was washed with water and dried over brine and Na_2SO_4. The solvents were evaporated under reduced pressure to give the crude product, which was purified by column chromatography on silica gel in 5% methanol/CH_2Cl_2 to give Example **9a** as a solid (2.1g, 4.0mmol, 54%). ^{1}HNMR (300 MHz, $CDCl_3$) 0.7-0.9 (m, 9H), 1.0-2.0 (m, 17H), 2.3-2.6 (m, 4H), 2.8 (m, 1H), 3.5-3.7 (m, 1H), 3.8-4.2 (m, 2H), 4.4-4.6 (m, 2H), 4.6-4.8 (m, 1H), 5.7-5.9 (m, 2H), 6.2-6.4 (m, 1H), 7.2-7.4 (m, 5H). MS: 527.3 (M+H), 549.3 (M+Na).

Example 9b.

3-(2-Benzyloxy-5-oxo-2,3,5,6,7,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-6-ylcarbamoyl)-5-methyl-2-propyl-hexanoic acid.

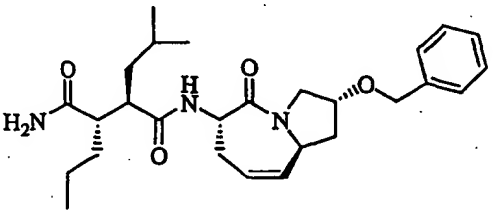


Example 9b

Example 9a (2.0g, 3.8mmol) was dissolved in 50ml of 50% TFA in CH_2Cl_2 and stirred at room temperature for 2 hours. The solvents were removed under reduced pressure and the resulting oil was redissolved in 50ml of toluene and concentrated to give acid Example 9b (1.7g, 3.6mmol), which was used without purification.

Example 9c.

N1-(2-Benzyloxy-5-oxo-2,3,5,6,7,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide.



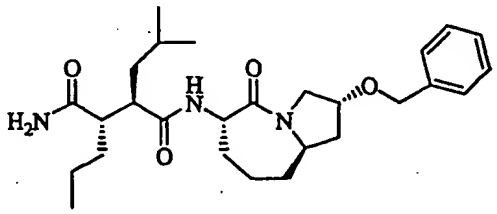
Example 9c

To a solution of Example 9b (1.7g, 3.6mmol) in 100ml DMF was added HATU (1.5g, 3.9mmol), followed by DIPEA (0.8ml, 4.6mmol). The solution was treated with ammonia gas for 5 minutes, the the reaction mixture was stirred overnight. The solvents were removed under reduced pressure and the resulting solid was purified by column chromatography on silica gel using 5% methanol/CH_2Cl_2 to give Example 9c as a white solid (920mg, 1.96mmol, 54%). ^{1}HNMR (300 MHz, $CDCl_3$) 0.7-0.9 (m, 9H), 1.2-2.0(m, 8H), 2.4-2.6 (m, 4H), 2.8 (m, 1H), 3.6 (m, 1H), 3.8-3.9(m, 1H), 4.0-4.1 (m, 1H), 4.51 (s,

2H), 4.55-4.65 (m, 1H), 4.8 (m, 1H), 5.6-5.8(m, 3H), 6.0-6.1 (s, 1H), 6.5 (d, 1H), 7.2-7.4 (m, 5H). MS: 470.3 (M+H), 492.2 (M+Na).

Example 10a.

N1-(2-Benzyloxy-5-oxo-octahydro-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide.

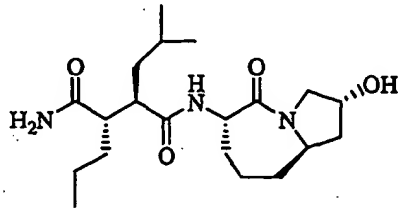


Example 10a

A solution of Example **9c** (100mg, 0.21mmol) in 30ml ethanol with 10mg Wilkinson's catalyst, (chlorotris(triphenylphosphine)rhodium(I)), was shaken under H_2 (~50psi) overnight. The solvent was removed under reduced pressure to give a slightly yellow solid. The crude product was purified by column chromatography on silica gel in 5% methanol/ CH_2Cl_2 to give Example **10a** as a white solid (60mg, 0.13mmol, 60%). ^{1}HNMR (300 MHz, CD_3OD) 0.7-0.9 (m, 9H), 0.9-1.1 (m, 1H), 1.1-1.4 (m, 3H), 1.4-1.6 (m, 4H), 1.6-2.0 (m, 5H), 2.0-2.2 (m, 1H), 2.3-2.4 (m, 2H), 2.4-2.6 (m, 1H), 3.4-3.6 (m, 1H), 3.6-3.8 (m, 1H), 4.0-4.2 (m, 2H), 4.4-4.6 (m, 3H), 7.2-7.4 (m, 5H). MS: 472.3 (M+H), 494.3 (M+Na).

Example 10b.

N1-(2-Hydroxy-5-oxo-octahydro-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide.



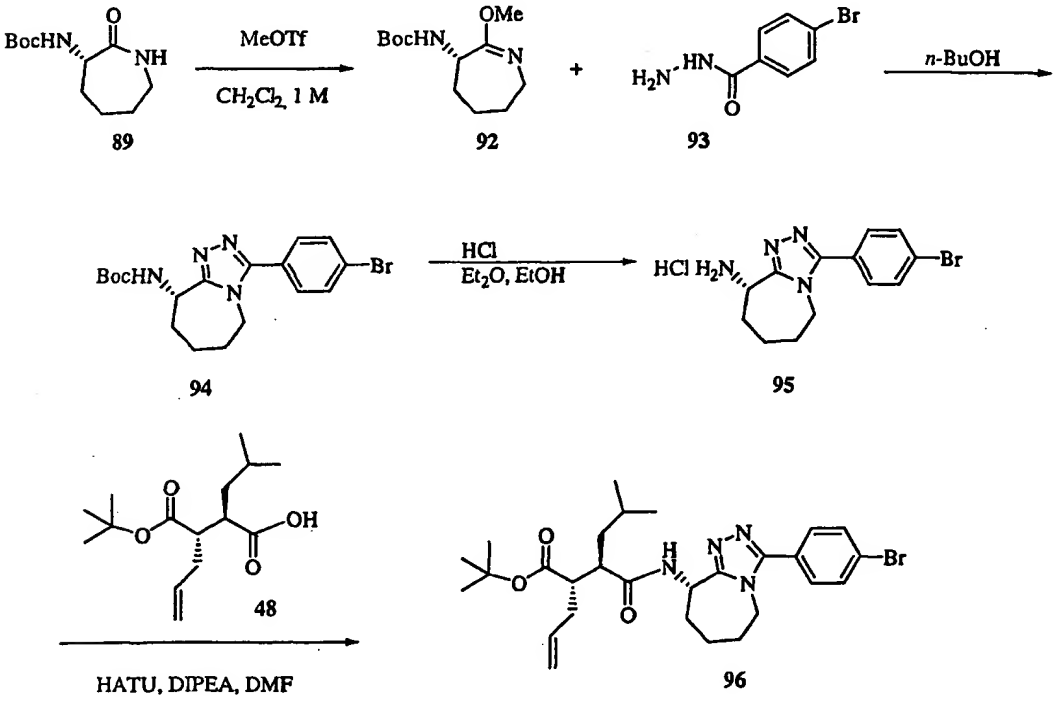
Example **10b**

A solution of Example **10a** (50mg, 0.11mmol) in 30ml ethanol was shaken under H_2 (~50psi) for 2hrs in the presence of 5mg Pd/C (5% on activated carbon). The reaction mixture was filtered, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel in 5% methanol/CH_2Cl_2 to give alcohol Example **10b** as a white solid (40mg, 0.10mmol, 90%). ^{1}HNMR (300MHz, CD_3OD) 0.8-0.9 (m, 9H), 1.0-2.0 (m, 15H), 2.0-2.2 (m, 2H), 2.2-2.4 (m, 1H), 2.5-2.7 (m, 1H), 3.4-3.6 (m, 3H), 4.0-4.2 (m, 1H), 4.3 (s, 1H), 4.5 (d, 1H). MS: 382.3 (M+H), 404.2 (M+Na).

For Examples 91-105, HPLC analyses were obtained using a Rainin Dynamax® C_{18} column with UV detection at 223 nm using a standard solvent gradient program unless specified otherwise.

Example 96

Preparation of 2-allyl-3-[3-(4-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester.



Preparation of compound **92.**

To a solution of compound **89** (16.8 g, 73.7 mmol) in CH_2Cl_2 (75 mL) at room temperature was added MeOTf (14.1 g, 85.9 mmol) and the solution was stirred for 6 h under N_2. The solution was then diluted with additional CH_2Cl_2 (200 mL), washed with sat. $NaHCO_3$ (3 x 300 mL), brine, and dried over anhydrous Na_2SO_4. The solution was filtered and concentrated to yield **92** (15.8 g, 88%) as a light yellow, viscous oil that was used without additional purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.42 (m, 1 H), 4.59 (m, 1 H), 3.71 (m, 4 H), 3.22 (t, J = 13.7 Hz, 1 H), 2.01-1.22 (m, 15 H); ESI MS m/z = 243 $[C_{13}H_{22}NO_3+H]^+$.

Preparation of compound **94.**

A solution of compound **92** (3.6 g, 14.7 mmol) and 4-bromobenzoic hydrazide, **93**, (3.0 g 13.9 mmol) in n-BuOH (100 mL) was heated at reflux for 24 h. The solvent was removed under reduced pressure and the resulting residue was purified by column chromatography (silica gel, 98:2 CH_2Cl_2/MeOH) to yield **94** (3.6 g, 60%) as a pale green solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78-7.39 (m, 4 H), 6.26 (s, 1 H), 4.86 (m, 1 H), 4.27 (m, 1 H), 3.74 (t, J = 13.7 Hz, 1 H), 2.47-1.41 (m, 15 H); ESI MS m/z = 407 $[C_{18}H_{23}BrN_4O_2+H]^+$.

Preparation of compound **95.**

A solution of compound **94** (1.2 g, 2.9 mmol), in ethanol (75 mL) and a 1 N solution of HCl in ether (75 mL) were stirred for 3 h. The solution was concentrated under reduced pressure and ether was added to the residue. The solid that precipitated was collected and dried under vacuum to yield **95** (0.81 g, 91%) as a tan solid: ^{1}H NMR (300 MHz, CD_3OD) δ 7.99-7.60 (m, 4 H), 4.47 (m, 1 H), 4.14 (m, 2 H), 2.39-1.35 (m, 6 H); ESI MS m/z = 307 $[C_{13}H_{15}BrN_4+H]^+$.

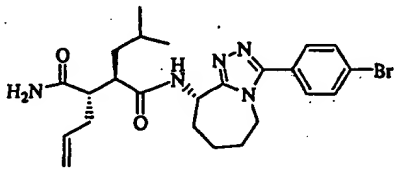
Preparation of Example **96.**

To a solution of **95** (1 g, 2.9 mmol), DIPEA (2.0 mL, 11.6 mmol) and **48** (0.63 g, 2.3 mmol) in DMF (30 mL) was added HATU (1.3 g, 3.5 mmol) and the solution was stirred at room temperature for 18 h. The resulting solution was partitioned between EtOAc (200 mL) and 5% LiCl (200 mL), the layers separated, the organic layer washed with 5% LiCl (2 x 100 mL), 0.1 N HCl (2 x 100 mL), sat. $NaHCO_3$ (2 x 100 mL), brine

(1 x 100 mL), and dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield an oily solid. This residue was further purified by column chromatography (silica gel, 70:30 EtOAc/hexanes) to yield 96 (0.66 g, 51%) as a white powder: mp 75-82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74-7.42 (m, 4 H), 5.77 (m, 1 H), 5.19-5.02 (m, 3 H), 4.23 (m, 1 H), 3.76 (t, J = 14.1 Hz, 1 H), 2.62-1.03 (m, 13 H), 0.95 (d, J = 7.0 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H); IR (KBr) 3406, 2932, 1726, 1671, 1490 cm^{-1}; ESI MS m/z = 559 $[C_{28}H_{39}BrN_4O_3+H]^+$; HPLC 100%, t_r = 22.68 min.

Example 91a

3-Allyl-N^1-[3-(4-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.

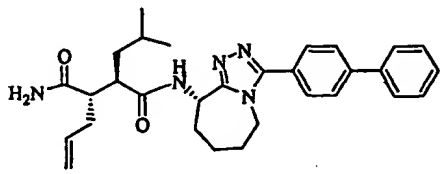


91a

To a solution of Example **96** (0.21 mg, 0.37 mmol) in CH_2Cl_2 (7 mL) was added TFA (7 mL) and the solution was allowed to stir for 24 h at room temperature. The solution was concentrated under reduced pressure, the residue was dissolved in CH_2Cl_2 (150 mL) and the solution was washed with $NaHCO_3$ (2 x 150 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated to yield a residue. Ammonia gas was bubbled through a solution of the foregoing residue (90 mg, 0.2 mmol) with DIPEA (0.12 mL, 0.71 mmol), HATU (82 mg, 0.214 mmol) in DMF for 30 min and the solution was allowed to stir for 24 h at room temperature. The contents of the flask were partitioned between EtOAc and a 5% LiCl solution (150 mL each), the organic phase washed with 5% LiCl (3 x 50 mL), and dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield a white solid. This was further purified by column chromatography (silica gel, 97:3 EtOAc/MeOH) to yield **91a** (45 mg, 24%) as a white powder: mp 159-166 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (s, 1 H), 7.78-7.44 (m, 4 H), 6.49 (s, 1 H), 6.07 (m, 1 H), 5.82 (m, 1 H), 5.31-4.96 (m, 3 H), 4.31 (m, 1 H) 3.86 (t, J = 14.1 Hz, 1 H), 2.89-1.22 (m, 13 H), 0.95 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 7.1 Hz, 3 H); IR (KBr) 3334, 2953, 1663, 1490, 1438 cm^{-1}; ESI MS m/z = 502 $[C_{24}H_{32}BrN_5O_2+H]^+$; HPLC 100%, t_r = 20.12 min.

Example 91b

3-Allyl-N[1]-[3-(4-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.



91b

Preparation of 2-allyl-3-[3-(4-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester.

To a solution of **96** (0.14 g, 0.24 mmol), Ph_3P (38 mg, 0.15 mmol), K_3PO_4 (0.26 g, 1.21 mmol), $PhB(OH)_2$ (44 mg, 0.36 mmol) in DMF/H_2O (5 mL:1 mL) was added $Pd(Ph_3P)_2Cl_2$ (50 mg, 0,07 mmol), and argon was bubbled through the solution for 30 min. The solution was heated to 70 °C for 10 h under Ar. The resulting solution was diluted with EtOAc (100 mL) washed with 5% LiCl (3 x 100 mL), and dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield a pale yellow waxy solid. This solid was further purified by column chromatography (silica gel, 50:50 EtOAc/hexanes) to yield **98b** (48 mg, 36%) as a white powder: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81-7.41 (m, 10 H), 5.73 (m, 1 H), 5.21-5.05 (m, 3 H), 4.42 (m, 1 H), 3.73 (t, *J* = 14.0 Hz, 1 H), 2.89-1.22 (m, 22 H), 0.92 (m, 6 H); ESI MS *m/z* = 557 $[C_{34}H_{44}N_4O_3+H]^+$.

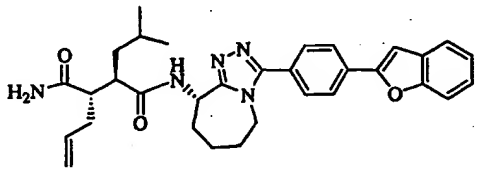
Preparation of Example **91b**.

To a solution of **98b** (45 mg, 0.08 mmol) in CH_2Cl_2 (5 mL) was added TFA (0.12 mL) and the solution was allowed to stir for 24 h at room temperature. The solution was concentrated under reduced pressure, the residue was redissolved in toluene and concentrated (3 x 10 mL). Ammonia gas was bubbled through a solution of the foregoing residue (30 mg, 0.06 mmol), DIPEA (0.05 mL, 0.3 mmol), HATU (46 mg, 0.12 mmol) in DMF (5 mL) for 30 min and the solution was allowed to stir for 24 h at room temperature. The contents of the flask were partitioned between EtOAc and a 5% LiCl solution (150 mL each), the organic phase washed with 5% LiCl (3 x 50 mL), and

dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield a white solid. This was further purified by column chromatography (silica gel, 97:3 EtOAc/MeOH) to yield **91b** (20 mg, 50%) as a white powder: mp 272-275 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82-7.38 (m, 10 H), 6.28 (s, 1 H), 5.84 (m, 1 H), 5.62 (s, 1 H), 5.28-4.99 (m, 3 H), 4.30 (m, 1 H), 3.87 (t, J = 14.0 Hz, 1 H), 2.89-1.22 (m, 13 H), 0.95 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 7.1 Hz, 3 H); IR (KBr) 3390, 2921, 1654, 1483, 1438 cm^{-1}; ESI MS m/z = 500 $[C_{30}H_{37}N_5O_2+H]^+$; HPLC 95.3%, t_r = 16.84 min.

Example 91c

3-Allyl-N^1- [3-(4-benzofuran-2-yl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.



91c

Preparation of 2-allyl-3-[3-(4- benzofuran-2-yl -phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester.

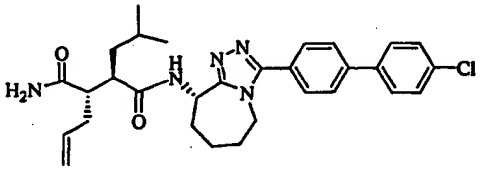
To a solution of **96** (0.112 g, 0.2 mmol), Ph_3P (10 mg, 0.04 mmol), K_3PO_4 (0.21 g, 1.0 mmol), benzo[b]furan-2-boronic acid (65 mg, 0.4 mmol) in DMF/H_2O (4 mL:1 mL) was added $Pd(Ph_3P)_2Cl_2$ (28 mg, 0.04 mmol), and argon was bubbled through the solution for 30 min. The solution was heated to 70 °C for 10 h under Ar. The resulting solution was diluted with EtOAc (100 mL), washed with 5% LiCl (3 x 100 mL), and dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield a white oily solid. This solid was further purified by column chromatography (silica gel, 50:50 EtOAc/hexanes) to yield **98c** (47 mg, 39%) as a white powder: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (m, 2 H), 7.62-7.17 (m, 8 H), 5.63 (m, 1 H), 5.09-4.90 (m, 3 H), 4.25 (m, 1 H), 3.69 (t, J = 13.8 Hz, 1 H), 2.59-1.09 (m, 22 H), 0.88 (d, J = 6.9 Hz, 3 H); 0.81 (d, J = 6.9 Hz, 3 H); ESI MS m/z = 597 $[C_{36}H_{44}N_4O_4+H]^+$.

Preparation of Example **91c.**

To a solution of **98c** (41 mg, 0.069 mmol) in CH_2Cl_2 (4 mL) was added TFA (4 mL) and the solution was allowed to stir for 24 h at room temperature. The solution was concentrated under reduced pressure, the residue was redissolved in toluene and concentrated (3 x 10 mL). Ammonia gas was bubbled through a solution of the foregoing residue (30 mg, 0.06 mmol), DIPEA (0.06 mL, 0.3 mmol), and HATU (29 mg, 0.08 mmol) in DMF (5 mL) for 30 min and the solution was allowed to stir for 24 h at room temperature. After the contents of the flask were partitioned between EtOAc and a 5% LiCl solution (50 mL each), the organic phase was washed with 5% LiCl (3 x 50 mL), and dried over anhydrous Na_2SO_4. Concentration gave a white solid which was further purified by column chromatography (silica gel, 97:3 EtOAc/MeOH) to yield **91c** (22 mg, 59%) as a white powder: mp 281-284 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (m, 2 H), 7.82-7.38 (m, 8 H), 6.07 (s, 1 H), 5.82 (m, 1 H), 5.37 (s, 1 H), 5.18-5.09 (m, 3 H), 4.42 (m, 1 H) 3.87 (t, J = 14.2 Hz, 1 H), 2.71-1.39 (m, 13 H), 1.00 (d, J = 7.1 Hz, 3 H), 0.92 (d, J = 7.1 Hz, 3 H); IR (KBr) 3303, 2928, 1664, 1641, 1438 cm^{-1}; ESI MS *m/z* = 540 $[C_{32}H_{37}N_5O_2+H]^+$; HPLC 96.2%, t_r = 17.72 min.

Example 91d

3-Allyl-N^1- [3-(4-(4-chloro-phenyl)-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.



91d

Preparation of 2-allyl-3-[3-(4-(4-chloro-phenyl)-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester.

To a solution of **96** (0.15 g, 0.25 mmol), Ph_3P (20 mg, 0.08 mmol), K_3PO_4 (0.27 g, 1.3 mmol), and 4-chlorophenyl boronic acid (59 mg, 0.38 mmol) in DMF/H_2O (8 mL:2 mL) was added $Pd(Ph_3P)_2Cl_2$ (53 mg, 0.07 mmol). Argon was bubbled through the solution for 30 min. The solution was heated to 70 °C for 10 h under Ar, then cooled, was diluted with EtOAc (100 mL), washed with 5% LiCl (3 x 100 mL), and dried over

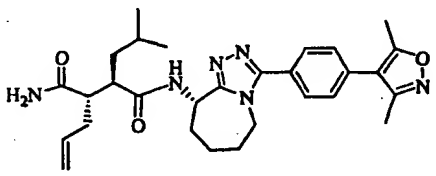
anhydrous Na_2SO_4. Filtration and concentration gave a light brown waxy solid. This solid was further purified by column chromatography (silica gel, 50:50 EtOAc/hexanes) to yield **98d** (68 mg, 46%) as a white powder: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83-7.41 (m, 10 H), 5.78 (m, 1 H), 5.20-5.02 (m, 3 H), 4.38 (m, 1 H), 3.76 (t, J = 14.0 Hz, 1 H), 2.59-1.02 (m, 22 H), 0.93 (d, J = 6.7 Hz, 3 H); 0.86 (d, J = 6.7 Hz, 3 H); ESI MS m/z = 591 $[C_{34}H_{43}ClN_4O_3+H]^+$.

Preparation of Example **91d.**

To a solution of **98d** (65 mg, 0.11 mmol) in CH_2Cl_2 (6 mL) was added TFA (2 mL) and the solution was allowed to stir for 24 h at room temperature. The solution was concentrated under reduced pressure, and the residue was redissolved in toluene and concentrated (3 x 10 mL). Ammonia gas was bubbled through a solution of the foregoing residue (55 mg, 0.1 mmol), DIPEA (0.1 mL, 0.59 mmol), HATU (90 mg, 0.24 mmol) in DMF (5 mL) for 30 min and the solution was allowed to stir for 24 h at room temperature. The contents of the flask were partitioned between EtOAc and a 5% LiCl solution (50 mL each), the organic phase washed with 5% LiCl (3 x 50 mL), and dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield a white solid. This was further purified by column chromatography (silica gel, 97:3 CH_2Cl_2/MeOH) to yield **91d** (33 mg, 56%) as a white powder: mp 262-267 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 8.82 (m, 1 H), 7.72-7.39 (m, 8 H), 5.53 (m, 1 H), 5.11 (s, 1 H), 4.92-4.75 (m, 3 H), 4.10 (m, 1 H), 3.87 (m, 1 H), 2.58-0.92 (m, 13 H), 0.79 (d, J = 7.2 Hz, 3 H), 0.71 (d, J = 7.2 Hz, 3 H); IR (KBr) 3405, 2954, 1655, 1486, 1467 cm^{-1}; ESI MS m/z = 534 $[C_{30}H_{36}ClN_5O_2+H]^+$; HPLC 95.8%, t_r = 16.56 min.

Example 91e

3-Allyl-N^1-[3-(4-(3,5-dimethylisoxazol-4-yl)phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.



91e

Preparation of 2-allyl-3-[3-(4-(3,5-dimethylisoxazol-4-yl)phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester.

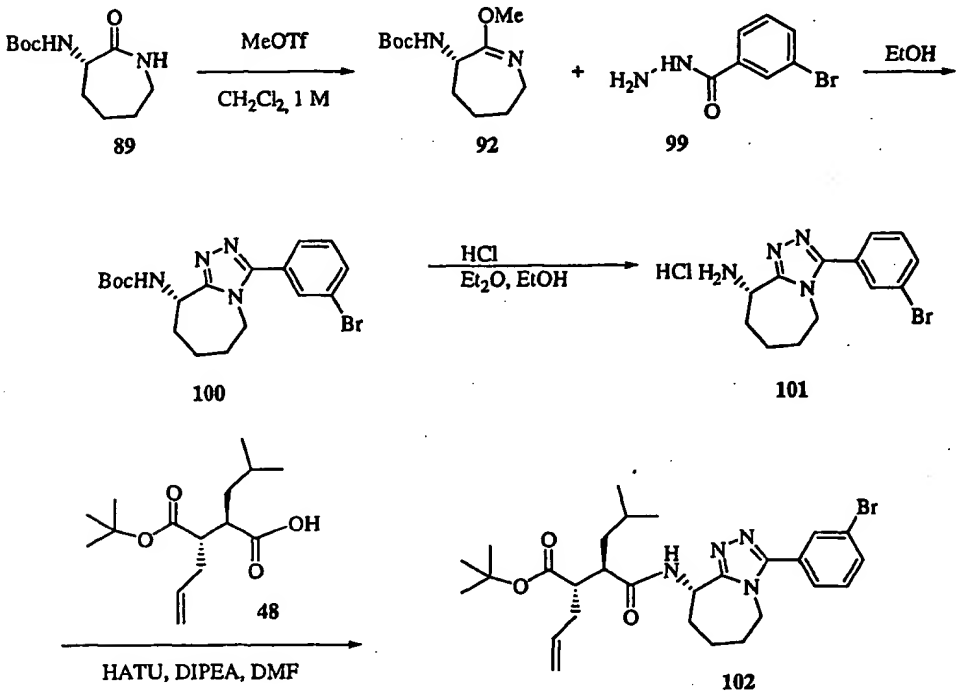
To a solution of **96** (0.12 g, 0.21 mmol), Ph_3P (11 mg, 0.04 mmol), K_3PO_4 (0.23 g, 1.1 mmol), and 3,5-dimethylisoxazole-4-boronic acid (60 mg, 0.43 mmol) in DMF/H_2O (5 mL:1 mL) was added $Pd(Ph_3P)_2Cl_2$ (50 mg, 0,07 mmol), and argon was bubbled through the solution for 30 min. The solution was heated to 70 °C for 10 h under Ar, then cooled, diluted with EtOAc (100 mL), washed with 5% LiCl (3 x 100 mL), and dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield a tan granular solid which was further purified by column chromatography (silica gel, 50:50 EtOAc/hexanes) to yield **98e** (48 mg, 40%) as a white powder: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.49 (m, 5 H), 5.82 (m, 1 H), 5.20-4.98 (m, 3 H), 4.36 (m, 1 H), 3.79 (t, J = 13.9 Hz, 1 H), 2.67-1.12 (m, 28 H), 0.98 (d, J = 6.9 Hz, 3 H); 0.91 (d, J = 6.9 Hz, 3 H); ESI MS m/z = 576 $[C_{33}H_{45}N_5O_4+H]^+$.

Preparation of Example **91e.**

To a solution of **98e** (48 mg, 0.08 mmol) in CH_2Cl_2 (6 mL) was added TFA (1 mL) and the solution was allowed to stir for 24 h at room temperature. The solution was concentrated under reduced pressure, the residue was redissolved in toluene and concentrated (3 x 10 mL). Ammonia gas was bubbled through a solution of the foregoing residue (30 mg, 0.05 mmol), DIPEA (0.044 mL, 0.25 mmol), and HATU (38 mg, 0.1 mmol) in DMF (5 mL) for 30 min and the solution was allowed to stir for 24 h at room temperature. The contents of the flask were partitioned between EtOAc and 5% LiCl solution (50 mL each), and the organic phase washed with 5% LiCl (3 x 50 mL), then dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield a white solid. This was further purified by column chromatography (silica gel, 97:3 CH_2Cl_2/MeOH) to yield **91e** (12 mg, 29%) as a white powder: mp 154-162 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72-7.39 (m, 5 H), 6.08 (m, 1 H), 5.80-5.76 (m, 1 H), 5.46 (m, 1 H), 5.16-5.04 (m, 3 H), 4.39 (m, 1 H), 3.81 (t, J = 13.8 Hz, 1 H), 2.68-1.25 (m, 19 H), 0.96 (d, J = 6.7 Hz, 3 H), 0.89 (d, J = 6.7 Hz, 3 H); IR (KBr) 3406, 2954, 2928, 1663, 1490 cm^{-1}; ESI MS m/z = 519 $[C_{29}H_{38}N_6O_3+H]^+$; HPLC 95.6%, t_r = 16.70 min.

Example 102

Preparation of 2-allyl-3-[3-(3-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester.



Preparation of compound **100.**

A solution of compound **92** (3.8 g, 14.7 mmol) and 3-bromobenzoic hydrazide, **99**, (3.0 g, 13.9 mmol) in EtOH (100 mL) was heated at reflux for 24 h. The solvent was removed under reduced pressure and the resulting residue was purified by column chromatography (silica gel, 98:2 CH_2Cl_2/MeOH) to yield **100** (4.0 g, 62%) as a pale green solid: ^{1}H NMR (300 MHz, $CDCl_3$) 7.71-7.38 (m, 4 H), 6.26 (s, 1 H), 4.91 (m, 1 H), 4.26 (m, 1 H), 3.73 (t, J = 14.1 Hz, 1 H), 2.47-1.41 (m, 15 H); ESI MS m/z = 407 $[C_{18}H_{23}BrN_4O_2+H]^+$.

Preparation of compound **101.**

A solution of compound **100** (3.3 g, 8.3 mmol), in ethanol (100 mL) was stirred with a 1 N solution of HCl in ether (150 mL) for 36 h. The solution was concentrated under reduced pressure and ether was added to the residue. The solid that precipitated was filtered and dried under vacuum to yield **101** (2.3 g, 89%) as a tan solid: ^{1}H NMR

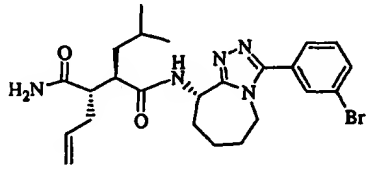
(300 MHz, CD_3OD) 8.03-7.75 (m, 4 H), 4.47 (m, 1 H), 4.14 (m, 2 H), 2.39-1.35 (m, 6 H); ESI MS *m/z* = 307 $[C_{13}H_{15}BrN_4+H]^+$.

Preparation of Example **102.**

To a solution of **95** (1 g, 2.9 mmol), DIPEA (2.0 mL, 11.6 mmol) and **48** (0.63 g, 2.3 mmol), in DMF (30 mL) was added HATU (1.3 g, 3.5 mmol). The solution was stirred at room temperature for 18 h, then partitioned between EtOAc (200 mL) and 5% LiCl (200 mL). The organic layer washed with 5% LiCl (2 x 100 mL), 0.1 N HCl (2 x 100 mL), sat. $NaHCO_3$ (2 x 100 mL), brine (1 x 100 mL), and dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated to yield an oily solid. This residue was further purified by column chromatography (silica gel, 70:30 EtOAc/hexanes) to yield **102** (0.66 g, 51%) as a white powder: mp 75-82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74-7.42 (m, 4 H), 5.77 (m, 1 H), 5.19-5.02 (m, 3 H), 4.23 (m, 1 H), 3.76 (t, *J* = 14.1 Hz, 1 H), 2.62-1.03 (m, 13 H), 0.95 (d, *J* = 7.0 Hz, 3 H), 0.87 (d, *J* = 7.0 Hz, 3 H); ESI MS *m/z* = 559 $[C_{28}H_{39}BrN_4O_3+H]^+$.

Example 103

3-Allyl-N^1-[3-(3-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.

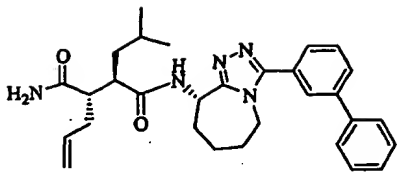


103

Example **103** was prepared using the procedures described for Example **91a.** ESI MS *m/z* = 502 $[C_{24}H_{32}BrN_5O_2+H]^+$.

Example 105a

3-Allyl-N^1-[3-(3-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.

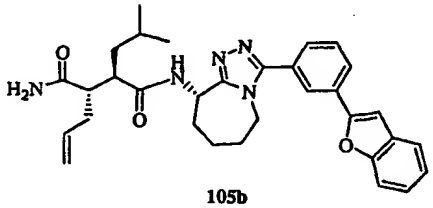


105a

Example **105a** was prepared in a manner similar to Example **91b** starting from compound **102**. Using the procedures disclosed in Example **91b**, compound **102** was reacted with phenyl boronic acid to form 2-allyl-3-[3-(3-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester; which was subsequently converted to the amide **105a**. ESI MS *m/z* = 500 $[C_{30}H_{37}N_5O_2+H]^+$.

Example 105b

3-Allyl-N^1-[3-(3-benzofuran-2-yl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.



105b

Example **105b** was prepared in a manner similar to Example **91c** starting from compound **102**. Using the procedures disclosed in Example **91c**, compound **102** was reacted with benzo[b]furan-2-boronic acid to form 2-allyl-3-[3-(3-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-ylcarbamoyl]-5-methyl-hexanoic acid *tert*-butyl ester; which was subsequently converted to the amide **105b**. ESI MS *m/z* = 540 $[C_{32}H_{37}N_5O_2+H]^+$.

UTILITY

Aβ production has been implicated in the pathology of Alzheimer's Disease (AD). The compounds of the present invention have utility for the prevention and treatment of AD by inhibiting Aβ production. Methods of treatment target formation of Aβ production through the enzymes involved in the proteolytic processing of β amyloid precursor protein. Compounds that inhibit β or γ secretase activity, either directly or indirectly, control the production of Aβ. Such inhibition of β or γ secretases reduces production of Aβ, and is expected to reduce or prevent the neurological disorders associated with Aβ protein, such as Alzheimer's Disease.

Cellular screening methods for inhibitors of Aβ production, testing methods for the *in vivo* suppression of Aβ production, and assays for the detection of secretase activity are known in the art and have been disclosed in numerous publications, including PCT publication number WO 98/22493, EPO publication number 0652009, US patent 5703129 and US patent 5593846; all hereby incorporated by reference.

The compounds of the present invention have utility for the prevention and treatment of disorders involving Aβ production, such as cerebrovascular disorders.

Compounds of the present invention have been shown to inhibit Aβ production, as determined by the secretase inhibition assay described below.

Compounds of the present invention have been shown to inhibit Aβ production, utilizing the C-terminus β amyloid precursor protein accumulation assay described below.

Compounds of Formula (I) are expected to possess γ secretase inhibitory activity. The γ secretase inhibitory activity of the compounds of the present invention is demonstrated using assays for such activity, for Example, using the assay described below. Compounds of the present invention have been shown to inhibit the activity of γ secretase, as determined by the Aβ immunoprecipitation assay.

Compounds provided by this invention should also be useful as standards and reagents in determining the ability of a potential pharmaceutical to inhibit Aβ production. These would be provided in commercial kits comprising a compound of this invention.

As used herein "μg" denotes microgram, "mg" denotes milligram, "g" denotes gram, "μL" denotes microliter, "mL" denotes milliliter, "L" denotes liter, "nM" denotes nanomolar, "μM" denotes micromolar, "mM" denotes millimolar, "M" denotes molar,

"nm" denotes nanometer, "SDS" denotes sodium dodecyl sulfate, and "DMSO" denotes dimethyl sulfoxide, and "EDTA" denotes ethylenediaminetetraacetato.

A compound is considered to be active if it has an IC_{50} or K_i value of less than about 100 μM for the inhibition of Aβ production or inhibition of proteolytic activity leading to Aβ production. Compounds, as demonstrated by use of the invention, have demonstrated IC_{50} values, for the inhibition of Aβ production, of less than about 100 μM. Preferably compounds, as demonstrated by use of the invention, demonstrate IC_{50} values, for the inhibition of Aβ production, of less than about 1 μM. More preferably compounds, as demonstrated by use of the invention, demonstrate IC_{50} values, for the inhibition of Aβ production, of less than about 100 nM. Even more preferably compounds, as demonstrated by use of the invention, demonstrate IC_{50} values, for the inhibition of Aβ production, of less than about 50 nM.

β Amyloid Precursor Protein Accumulation Assay (β APPA assay)

An assay to evaluate the accumulation of Aβ protein was developed to detect potential inhibitors of secretases. The assay uses the N 9 cell line, characterized for expression of exogenous APP by immunoblotting and immunoprecipitation.

The effect of test compounds on the accumulation of Aβ in the conditioned medium is tested by immunoprecipitation. N 9 cells are grown to confluency in 6-well plates and washed twice with 1 x Hank's buffered salt solution. The cells are starved in methionine/cysteine deficient media for 30 min., followed by replacement with fresh deficient media containing 150uCi Tran35S-LABEL™ (ICN). Test compounds dissolved in DMSO (final concentration 1%) are added, over a range of 1 picomolar to 100 micromolar, together with the addition of the fresh media containing Tran35S-LABEL™. The cells are incubated for 4 h at 37°C in a tissue culture incubator.

At the end of the incubation period, the conditioned medium is harvested and pre-cleared by the addition of 5 μl normal mouse serum and 50ul of protein A Sepharose (Pharmacia), mixed by end-over-end rotation for 30 minutes at 4°C, followed by a brief centrifugation in a microfuge. The supernatant is then harvested and transferred to fresh tubes containing 5ug of a monoclonal antibody (examples of antibodies include but are not limited by, clone 1101.1, directed against an internal peptide sequence in Aβ; or 6E10 from Senetek; or 4G8 from Senetek; additionally polyclonals from rabbit antihuman Aβ from Boehringer Mannheim) and 50 μl protein A Sepharose. After

incubation overnight at 4°C, the samples are washed three times with high salt washing buffer (50mM Tris, pH 7.5, 500mM NaCl, 5mM EDTA, 0.5% Nonidet P-40), three times with low salt wash buffer (50mM Tris, pH 7.5, 150mM NaCl, 5mM EDTA, 0.5% Nonidet P-40), and three times with 10mM Tris, pH 7.5. The pellet after the last wash is resuspended in SDS sample buffer (Laemmli U.K. Cleavage of structural proteins during the assembly of the head of bacteriphage T4. Nature 227, 680-5, 1970.) and boiled for 3 minutes. The supernatant is then fractionated on either 10-20% Tris/Tricine SDS gels or on 16.5% Tris/Tricine SDS gels. The gels are dried and exposed to X-ray film or analyzed by phosphorimaging. The resulting image is analyzed for the presence of Aβ polypeptides. The steady-state level of Aβ in the presence of a test compound is compared to wells treated with DMSO (1%) alone. A typical test compound in this assay blocks Aβ accumulation in the conditioned medium, and is considered active with an IC_{50} less than 100 μM.

C-Terminus b Amyloid Precursor Protein Accumulation Assay (CTF assay)

The effect of test compounds on the accumulation of C-terminal fragments is determined by immunoprecipitation of APP and fragments thereof from cell lysates. N 9 cells are metabolically labeled, as above, with media containing Tran35S-LABEL™, in the presence or absence of test compounds. At the end of the incubation period, the conditioned medium are harvested and cells lysed in RIPA buffer (10 mM Tris, pH 8.0 containing 1% Triton X-100, 1% deoxycholate, 0.1% SDS, 150mM NaCl, 0.125% NaN_3). Again, lysates are precleared with 5ul normal rabbit serum/50ul protein A Sepharose, followed by the addition of BC-1 antiserum (15μl;) and 50μl protein A Sepharose for 16 hours at 4°C. The immunoprecipitates are washed as above, bound proteins eluted by boiling in SDS sample buffer and fractionated by Tris/Tricine SDS-PAGE. After exposure to X-ray film or phosphorimager, the resulting images are analyzed for the presence of C-terminal APP fragments. The steady-state level of C-terminal APP fragments is compared to wells treated with DMSO (1%) alone. A typical test compound in this assay stimulates C-terminal fragment accumulation in the cell lysates, and is considered active with an IC_{50} less than 100 μM.

Accumulation-Release Assay

This immunoprecipitation assay is specific for g secretase activity (i.e., proteolytic activity required to generate the C-terminal end of Aβ either by direct cleavage or generating a C-terminal extended species which is subsequently further proteolyzed). N 9 cells are pulse labeled with media containing Tran35S-LABEL™ in the presence of a reported g secretase inhibitor (MDL 28170; Higaki J, Quon D, Zhong Z, Cordell B. Inhibition of beta-amyloid formation identifies proteolytic precursors and subcellular site of catabolism. Neuron 14, 651-659, 1995) for 1 h, followed by washing to remove ^{35}S radiolabel and MDL 28170. The media is replaced and test compounds are added over a dose range (for example 0.1nM to 100uM). The cells are chased for increasing periods of times and Aβ is isolated from the conditioned medium and C-terminal fragments from cell lysates (see accumulation assay above). The activity of test compounds are characterized by whether a stabilization of C-terminal fragments is observed and whether Aβ is generated from these accumulated precursor. A typical test compound in this assay prevents the generation of Aβ out of accumulated C-terminal fragments and is considered active with an IC_{50} less than 100 μM.

Dosage and Formulation

The compounds determined from the present invention can be administered orally using any pharmaceutically acceptable dosage form known in the art for such administration. The active ingredient can be supplied in solid dosage forms such as dry powders, granules, tablets or capsules, or in liquid dosage forms, such as syrups or aqueous suspensions. The active ingredient can be administered alone, but is generally administered with a pharmaceutical carrier. A valuable treatise with respect to pharmaceutical dosage forms is Remington's Pharmaceutical Sciences, Mack Publishing.

The compounds determined from the present invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions. Likewise, they may also be administered in intravenous (bolus or infusion), intraperitoneal, subcutaneous, or intramuscular form, all using dosage forms well known to those of ordinary skill in the pharmaceutical arts. An effective but non-toxic amount of the compound desired can be employed to prevent or treat neurological disorders related to β-amyloid production or accumulation, such as Alzheimer's disease and Down's Syndrome.

The compounds of this invention can be administered by any means that produces contact of the active agent with the agent's site of action in the body of a host, such as a human or a mammal. They can be administered by any conventional means available for use in conjunction with pharmaceuticals, either as individual therapeutic agents or in a combination of therapeutic agents. They can be administered alone, but generally administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage regimen for the compounds determined from the present invention will, of course, vary depending upon known factors, such as the pharmacodynamic characteristics of the particular agent and its mode and route of administration; the species, age, sex, health, medical condition, and weight of the recipient; the nature and extent of the symptoms; the kind of concurrent treatment; the frequency of treatment; the route of administration, the renal and hepatic function of the patient,and the effect desired. An ordinarily skilled physician or veterinarian can readily determine and prescribe the effective amount of the drug required to prevent, counter, or arrest the progress of the condition.

Advantageously, compounds determined from the present invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three, or four times daily.

The compounds identified using the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal routes, using those forms of transdermal skin patches wall known to those of ordinary skill in that art. To be administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittant throughout the dosage regimen.

In the methods of the present invention, the compounds herein described in detail can form the active ingredient, and are typically administered in admixture with suitable pharmaceutical diluents, excipients, or carriers (collectively referred to herein as carrier materials) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules, elixirs, syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic, pharmaceutically acceptable,

inert carrier such as lactose, starch, sucrose, glucose, methyl callulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol and the like; for oral administration in liquid form, the oral drug components can be combined with any oral, non-toxic, pharmaceutically acceptable inert carrier such as ethanol, glycerol, water, and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents, and coloring agents can also be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars such as glucose or β□lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth, or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum, and the like.

The compounds determined from the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamallar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine, or phosphatidylcholines.

Compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide-phenol, polyhydroxyethylaspartamidephenol, or polyethyleneoxide-polylysine substituted with palmitoyl residues. Furthermore, the compounds determined from the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacylates, and crosslinked or amphipathic block copolymers of hydrogels.

Gelatin capsules may contain the active ingredient and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric coated for selective disintegration in the gastrointestinal tract.

Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance.

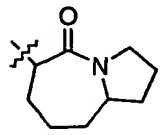
In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium EDTA. In addition, parenteral solutions can contain preservatives, such as benzalkonium chloride, methyl- or propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, Mack Publishing Company, a standard reference text in this field.

Table 1 demonstrates representative compounds envisaged within the scope of the present invention. Each formulae at the start of Table 1 are intended to be paired with each entry in the table which follows. The formulae are generated by combining each fragment from Group A with each fragment with Group B.

Table 1

Group A (each fragment in Group A has a -W-X-Y-Z group attached thereto, the fragment can be attached at any point on the multi-ring system)



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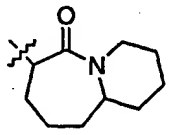

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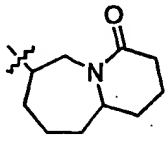

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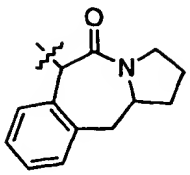

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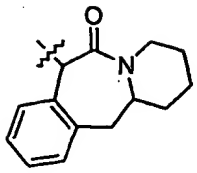

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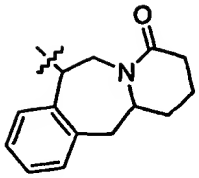

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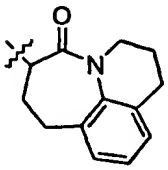

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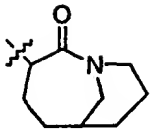

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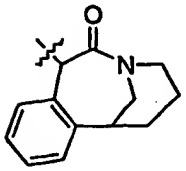

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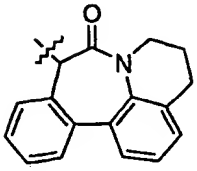

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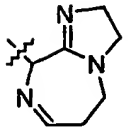

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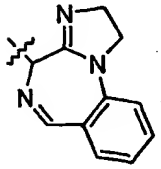

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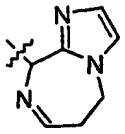

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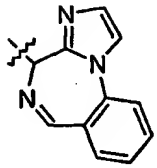

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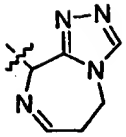

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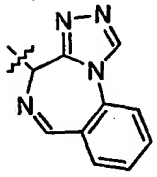

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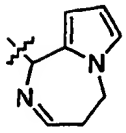

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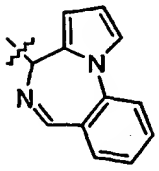

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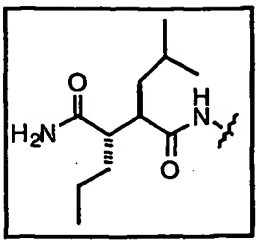
Group B



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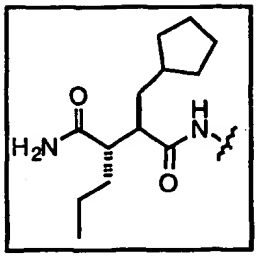

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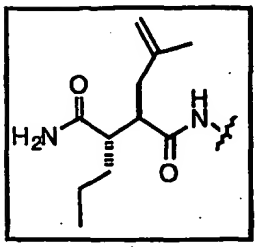

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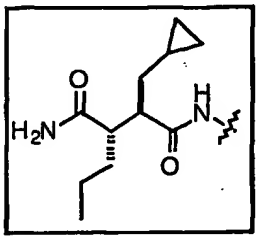

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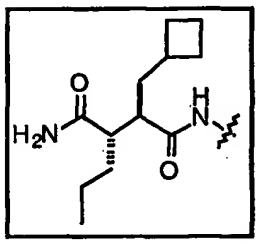

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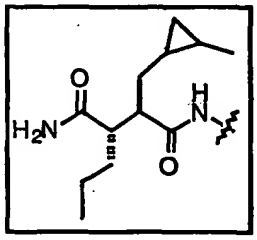

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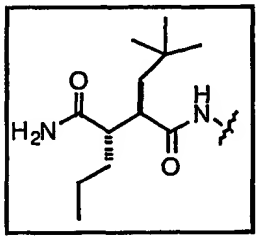

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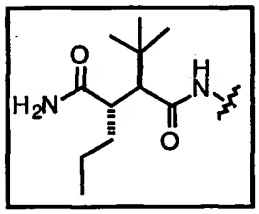

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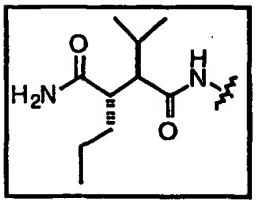

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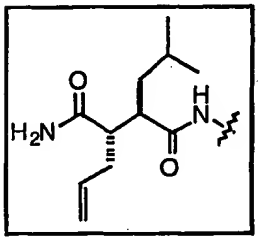

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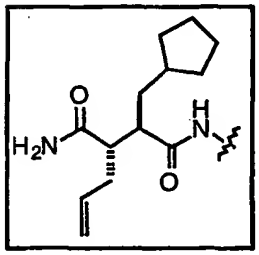

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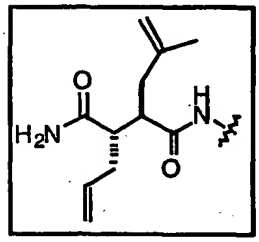

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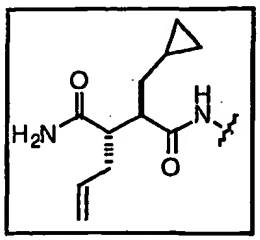

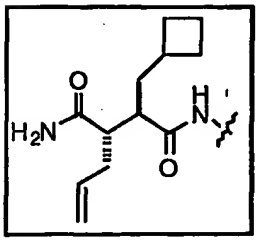

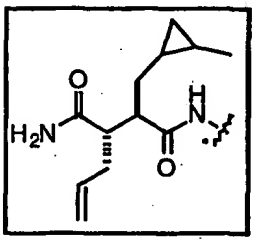

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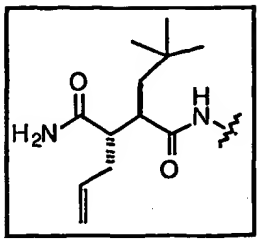

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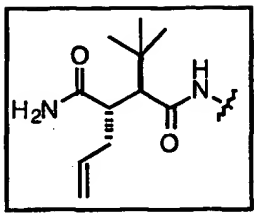

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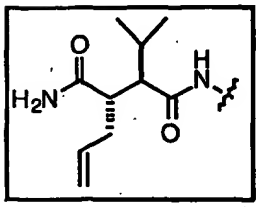

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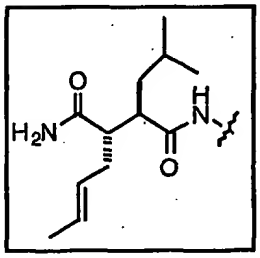

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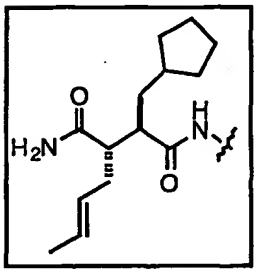

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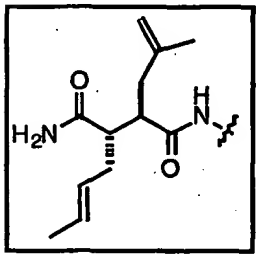

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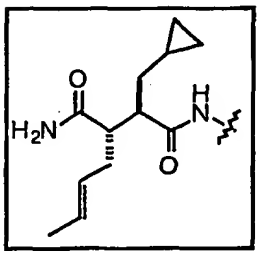

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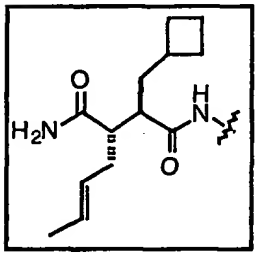

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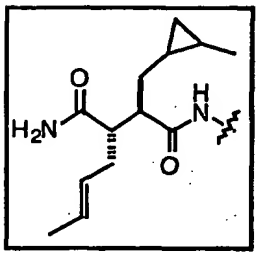

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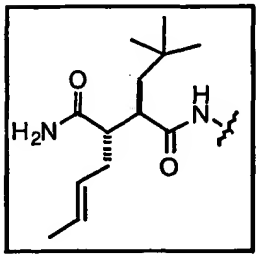

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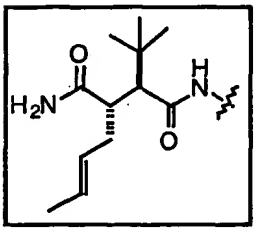

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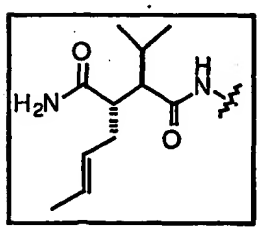

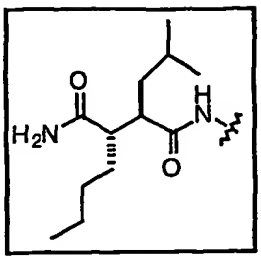

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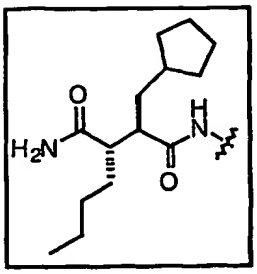

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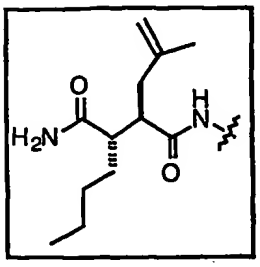

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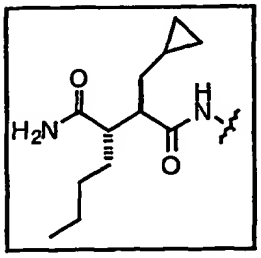

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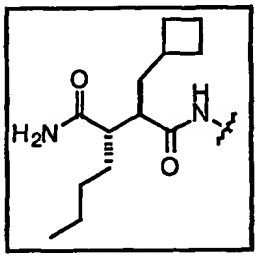

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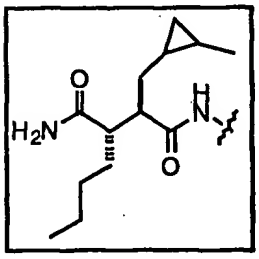

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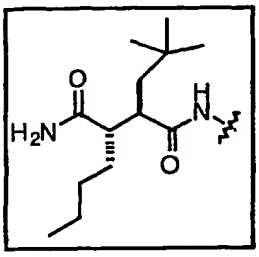

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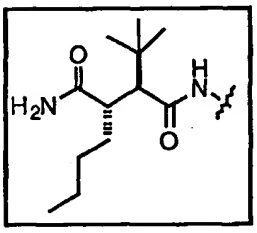

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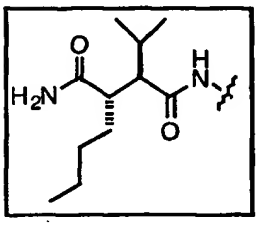

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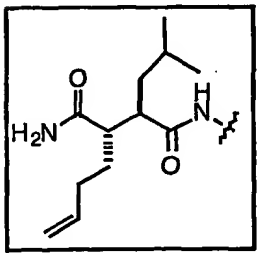

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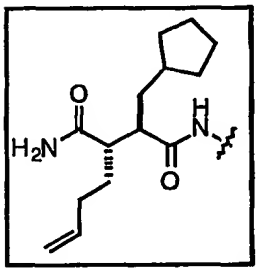

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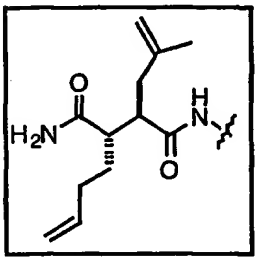

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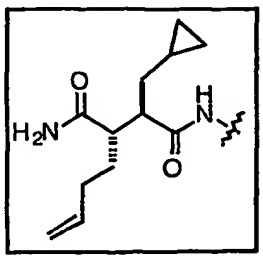

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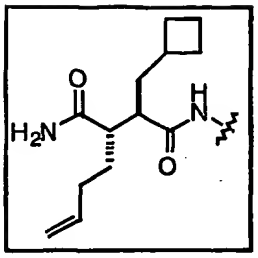

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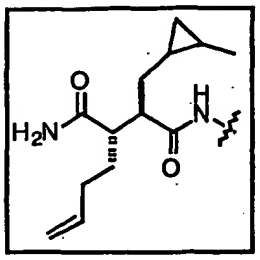

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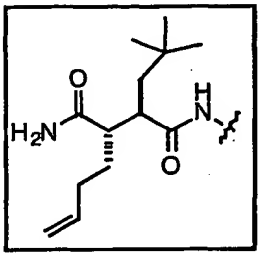

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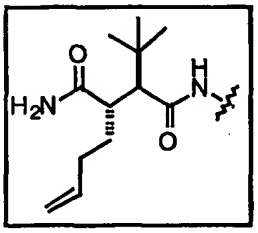

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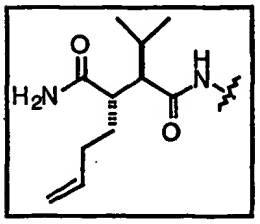

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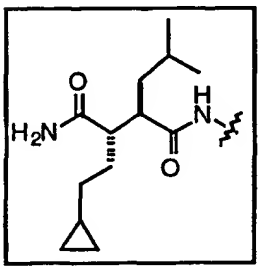

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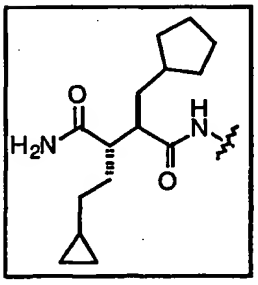

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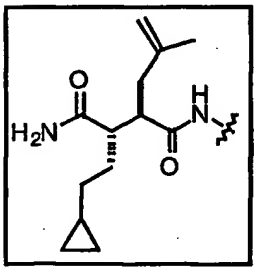

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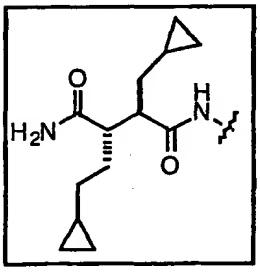

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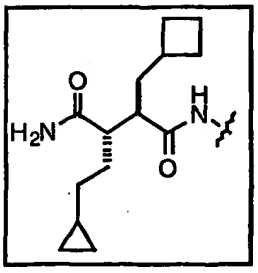

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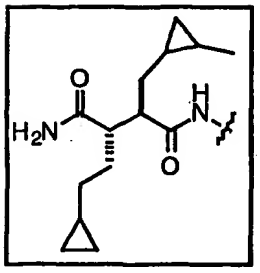

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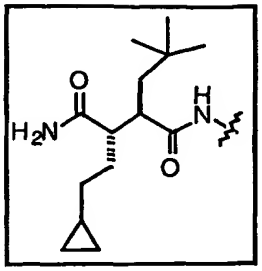

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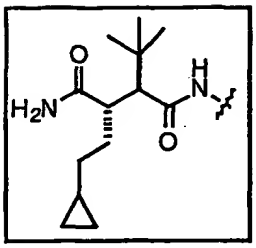

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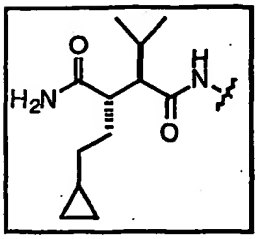

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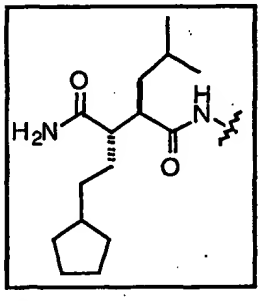

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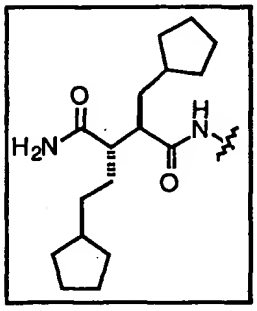

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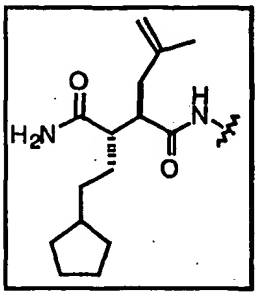

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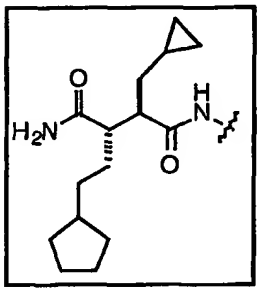

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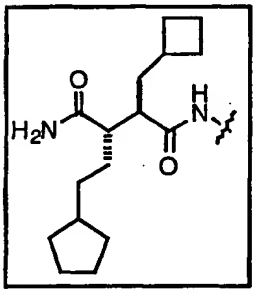

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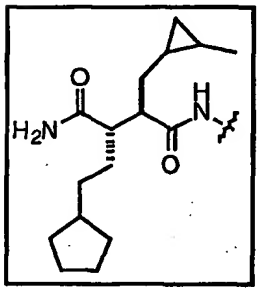

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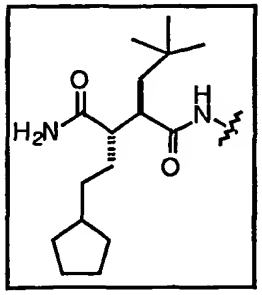

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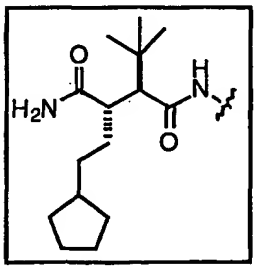

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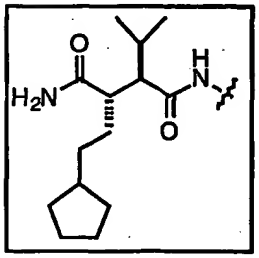

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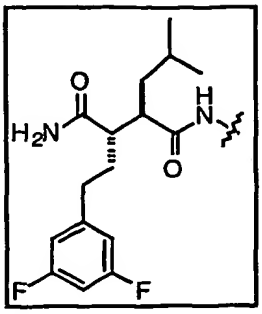

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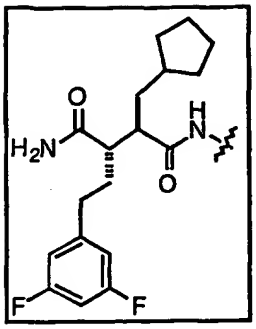

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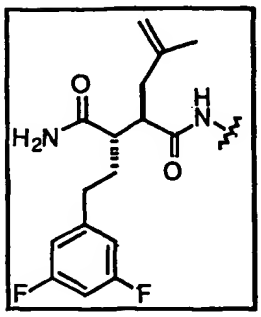

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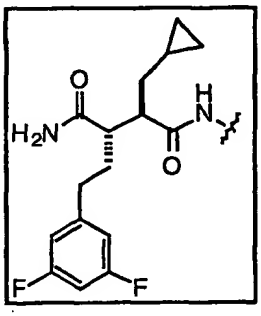

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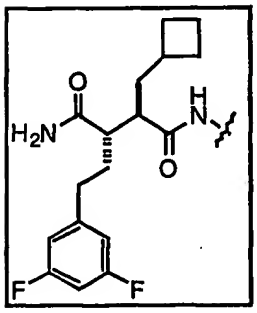

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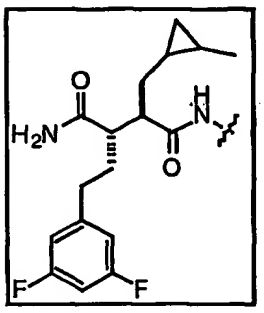

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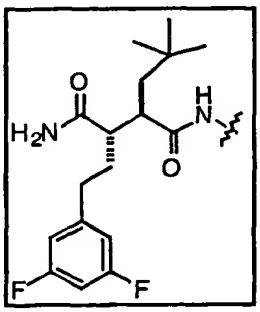

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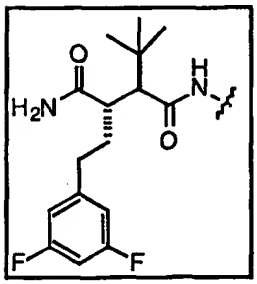

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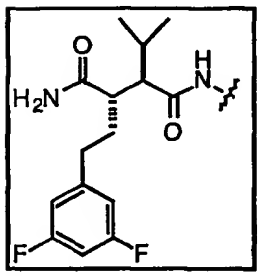

bt

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102	-CH_2-	phen-1,3-diyl	bond	2-F-phenyl
103	-CH_2-	phen-1,3-diyl	bond	3-F-phenyl
104	-CH_2-	phen-1,3-diyl	bond	4-F-phenyl
105	-CH_2-	phen-1,3-diyl	bond	2-Cl-phenyl

106	-CH_2-	phen-1,3-diyl	bond	3-Cl-phenyl
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108	-CH_2-	phen-1,3-diyl	bond	2-Me-phenyl
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110	-CH_2-	phen-1,3-diyl	bond	4-Me-phenyl
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112	-CH_2-	phen-1,3-diyl	bond	3-MeO-phenyl
113	-CH_2-	phen-1,3-diyl	bond	4-MeO-phenyl
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115	-CH_2-	phen-1,3-diyl	bond	3-MeS-phenyl
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118	-CH_2-	phen-1,3-diyl	bond	3-F_3C-phenyl
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123	-CH_2-	phen-1,3-diyl	bond	2,6-diF-phenyl
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127	-CH_2-	phen-1,3-diyl	bond	2,4-diCl-phenyl
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129	-CH_2-	phen-1,3-diyl	bond	2,6-diCl-phenyl
130	-CH_2-	phen-1,3-diyl	bond	3,4-diCl-phenyl
131	-CH_2-	phen-1,3-diyl	bond	3,5-diCl-phenyl
132	-CH_2-	phen-1,3-diyl	bond	2-Cl-3-F-phenyl
133	-CH_2-	phen-1,3-diyl	bond	2-Cl-4-F-phenyl
134	-CH_2-	phen-1,3-diyl	bond	2-Cl-5-F-phenyl
135	-CH_2-	phen-1,3-diyl	bond	3-Cl-4-F-phenyl
136	-CH_2-	phen-1,3-diyl	bond	3-Cl-5-F-phenyl
137	-CH_2-	phen-1,3-diyl	bond	4-Cl-2-F-phenyl
138	-CH_2-	phen-1,3-diyl	bond	4-Cl-3-F-phenyl
139	-CH_2-	phen-1,3-diyl	bond	2,3-diMeO-phenyl

140	-CH_2-	phen-1,3-diyl	bond	2,4-diMeO-phenyl
141	-CH_2-	phen-1,3-diyl	bond	2,5-diMeO-phenyl
142	-CH_2-	phen-1,3-diyl	bond	2,6-diMeO-phenyl
143	-CH_2-	phen-1,3-diyl	bond	3,4-diMeO-phenyl
144	-CH_2-	phen-1,3-diyl	bond	3,5-diMeO-phenyl
145	-CH_2-	phen-1,3-diyl	bond	cyclopropyl
146	-CH_2-	phen-1,3-diyl	bond	cyclobutyl
147	-CH_2-	phen-1,3-diyl	bond	cyclopentyl
148	-CH_2-	phen-1,3-diyl	bond	cyclohexyl
149	-CH_2-	phen-1,3-diyl	bond	2-furanyl
150	-CH_2-	phen-1,3-diyl	bond	2-thienyl
151	-CH_2-	phen-1,3-diyl	bond	2-imidazolyl
152	-CH_2-	phen-1,3-diyl	bond	2-pyridyl
153	-CH_2-	phen-1,3-diyl	bond	3-pyridyl
154	-CH_2-	phen-1,3-diyl	bond	4-pyridyl
155	-CH_2-	phen-1,3-diyl	bond	N-morpholinyl
156	-CH_2-	phen-1,3-diyl	bond	N-piperidinyl
157	-CH_2-	phen-1,3-diyl	bond	3-Me-2-pyridyl
158	-CH_2-	phen-1,3-diyl	bond	4-Me-2-pyridyl
159	-CH_2-	phen-1,3-diyl	bond	1-indolyl
160	-CH_2-	phen-1,3-diyl	bond	2-benzothienyl
161	-CH_2-	phen-1,3-diyl	bond	2-benzofuranyl
162	-CH_2-	phen-1,3-diyl	bond	1-benzimidazole
163	-CH_2-	phen-1,3-diyl	bond	2-naphthyl
164	-CH_2-	pyridin-3,5-diyl	bond	phenyl
165	-CH_2-	pyridin-3,5-diyl	bond	3,3-diphenylmethyl
166	-CH_2-	pyridin-3,5-diyl	bond	2-F-phenyl
167	-CH_2-	pyridin-3,5-diyl	bond	3-F-phenyl
168	-CH_2-	pyridin-3,5-diyl	bond	4-F-phenyl
169	-CH_2-	pyridin-3,5-diyl	bond	2-Cl-phenyl
170	-CH_2-	pyridin-3,5-diyl	bond	3-Cl-phenyl
171	-CH_2-	pyridin-3,5-diyl	bond	4-Cl-phenyl
172	-CH_2-	pyridin-3,5-diyl	bond	2-Me-phenyl
173	-CH_2-	pyridin-3,5-diyl	bond	3-Me-phenyl

174	-CH_2-	pyridin-3,5-diyl	bond	4-Me-phenyl
175	-CH_2-	pyridin-3,5-diyl	bond	2-MeO-phenyl
176	-CH_2-	pyridin-3,5-diyl	bond	3-MeO-phenyl
177	-CH_2-	pyridin-3,5-diyl	bond	4-MeO-phenyl
178	-CH_2-	pyridin-3,5-diyl	bond	2-MeS-phenyl
179	-CH_2-	pyridin-3,5-diyl	bond	3-MeS-phenyl
180	-CH_2-	pyridin-3,5-diyl	bond	4-MeS-phenyl
181	-CH_2-	pyridin-3,5-diyl	bond	2-F_3C-phenyl
182	-CH_2-	pyridin-3,5-diyl	bond	3-F_3C-phenyl
183	-CH_2-	pyridin-3,5-diyl	bond	4-F_3C-phenyl
184	-CH_2-	pyridin-3,5-diyl	bond	2,3-diF-phenyl
185	-CH_2-	pyridin-3,5-diyl	bond	2,4-diF-phenyl
186	-CH_2-	pyridin-3,5-diyl	bond	2,5-diF-phenyl
187	-CH_2-	pyridin-3,5-diyl	bond	2,6-diF-phenyl
188	-CH_2-	pyridin-3,5-diyl	bond	3,4-diF-phenyl
189	-CH_2-	pyridin-3,5-diyl	bond	3,5-diF-phenyl
190	-CH_2-	pyridin-3,5-diyl	bond	2,3-diCl-phenyl
191	-CH_2-	pyridin-3,5-diyl	bond	2,4-diCl-phenyl
192	-CH_2-	pyridin-3,5-diyl	bond	2,5-diCl-phenyl
193	-CH_2-	pyridin-3,5-diyl	bond	2,6-diCl-phenyl
194	-CH_2-	pyridin-3,5-diyl	bond	3,4-diCl-phenyl
195	-CH_2-	pyridin-3,5-diyl	bond	3,5-diCl-phenyl
196	-CH_2-	pyridin-3,5-diyl	bond	2-Cl-3-F-phenyl
197	-CH_2-	pyridin-3,5-diyl	bond	2-Cl-4-F-phenyl
198	-CH_2-	pyridin-3,5-diyl	bond	2-Cl-5-F-phenyl
199	-CH_2-	pyridin-3,5-diyl	bond	3-Cl-4-F-phenyl
200	-CH_2-	pyridin-3,5-diyl	bond	3-Cl-5-F-phenyl
201	-CH_2-	pyridin-3,5-diyl	bond	4-Cl-2-F-phenyl
202	-CH_2-	pyridin-3,5-diyl	bond	4-Cl-3-F-phenyl
203	-CH_2-	pyridin-3,5-diyl	bond	2,3-diMeO-phenyl
204	-CH_2-	pyridin-3,5-diyl	bond	2,4-diMeO-phenyl
205	-CH_2-	pyridin-3,5-diyl	bond	2,5-diMeO-phenyl
206	-CH_2-	pyridin-3,5-diyl	bond	2,6-diMeO-phenyl
207	-CH_2-	pyridin-3,5-diyl	bond	3,4-diMeO-phenyl

208	-CH_2-	pyridin-3,5-diyl	bond	3,5-diMeO-phenyl
209	-CH_2-	pyridin-3,5-diyl	bond	cyclopropyl
210	-CH_2-	pyridin-3,5-diyl	bond	cyclobutyl
211	-CH_2-	pyridin-3,5-diyl	bond	cyclopentyl
212	-CH_2-	pyridin-3,5-diyl	bond	cyclohexyl
213	-CH_2-	pyridin-3,5-diyl	bond	2-furanyl
214	-CH_2-	pyridin-3,5-diyl	bond	2-thienyl
215	-CH_2-	pyridin-3,5-diyl	bond	2-imidazolyl
216	-CH_2-	pyridin-3,5-diyl	bond	2-pyridyl
217	-CH_2-	pyridin-3,5-diyl	bond	3-pyridyl
218	-CH_2-	pyridin-3,5-diyl	bond	4-pyridyl
219	-CH_2-	pyridin-3,5-diyl	bond	N-morpholinyl
220	-CH_2-	pyridin-3,5-diyl	bond	N-piperidinyl
221	-CH_2-	pyridin-3,5-diyl	bond	3-Me-2-pyridyl
222	-CH_2-	pyridin-3,5-diyl	bond	4-Me-2-pyridyl
223	-CH_2-	pyridin-3,5-diyl	bond	1-indolyl
224	-CH_2-	pyridin-3,5-diyl	bond	2-benzothienyl
225	-CH_2-	pyridin-3,5-diyl	bond	2-benzofuranyl
226	-CH_2-	pyridin-3,5-diyl	bond	1-benzimidazole
227	-CH_2-	pyridin-3,5-diyl	bond	2-naphthyl
228	-CH_2-	pyridin-2,6-diyl	bond	phenyl
229	-CH_2-	pyridin-2,6-diyl	bond	3,3-diphenylmethyl
230	-CH_2-	pyridin-2,6-diyl	bond	2-F-phenyl
231	-CH_2-	pyridin-2,6-diyl	bond	3-F-phenyl
232	-CH_2-	pyridin-2,6-diyl	bond	4-F-phenyl
233	-CH_2-	pyridin-2,6-diyl	bond	2-Cl-phenyl
234	-CH_2-	pyridin-2,6-diyl	bond	3-Cl-phenyl
235	-CH_2-	pyridin-2,6-diyl	bond	4-Cl-phenyl
236	-CH_2-	pyridin-2,6-diyl	bond	2-Me-phenyl
237	-CH_2-	pyridin-2,6-diyl	bond	3-Me-phenyl
238	-CH_2-	pyridin-2,6-diyl	bond	4-Me-phenyl
239	-CH_2-	pyridin-2,6-diyl	bond	2-MeO-phenyl
240	-CH_2-	pyridin-2,6-diyl	bond	3-MeO-phenyl
241	-CH_2-	pyridin-2,6-diyl	bond	4-MeO-phenyl

242	-CH_2-	pyridin-2,6-diyl	bond	2-MeS-phenyl
243	-CH_2-	pyridin-2,6-diyl	bond	3-MeS-phenyl
244	-CH_2-	pyridin-2,6-diyl	bond	4-MeS-phenyl
245	-CH_2-	pyridin-2,6-diyl	bond	2-F_3C-phenyl
246	-CH_2-	pyridin-2,6-diyl	bond	3-F_3C-phenyl
247	-CH_2-	pyridin-2,6-diyl	bond	4-F_3C-phenyl
248	-CH_2-	pyridin-2,6-diyl	bond	2,3-diF-phenyl
249	-CH_2-	pyridin-2,6-diyl	bond	2,4-diF-phenyl
250	-CH_2-	pyridin-2,6-diyl	bond	2,5-diF-phenyl
251	-CH_2-	pyridin-2,6-diyl	bond	2,6-diF-phenyl
252	-CH_2-	pyridin-2,6-diyl	bond	3,4-diF-phenyl
253	-CH_2-	pyridin-2,6-diyl	bond	3,5-diF-phenyl
254	-CH_2-	pyridin-2,6-diyl	bond	2,3-diCl-phenyl
255	-CH_2-	pyridin-2,6-diyl	bond	2,4-diCl-phenyl
256	-CH_2-	pyridin-2,6-diyl	bond	2,5-diCl-phenyl
257	-CH_2-	pyridin-2,6-diyl	bond	2,6-diCl-phenyl
258	-CH_2-	pyridin-2,6-diyl	bond	3,4-diCl-phenyl
259	-CH_2-	pyridin-2,6-diyl	bond	3,5-diCl-phenyl
260	-CH_2-	pyridin-2,6-diyl	bond	2-Cl-3-F-phenyl
261	-CH_2-	pyridin-2,6-diyl	bond	2-Cl-4-F-phenyl
262	-CH_2-	pyridin-2,6-diyl	bond	2-Cl-5-F-phenyl
263	-CH_2-	pyridin-2,6-diyl	bond	3-Cl-4-F-phenyl
264	-CH_2-	pyridin-2,6-diyl	bond	3-Cl-5-F-phenyl
265	-CH_2-	pyridin-2,6-diyl	bond	4-Cl-2-F-phenyl
266	-CH_2-	pyridin-2,6-diyl	bond	4-Cl-3-F-phenyl
267	-CH_2-	pyridin-2,6-diyl	bond	2,3-diMeO-phenyl
268	-CH_2-	pyridin-2,6-diyl	bond	2,4-diMeO-phenyl
269	-CH_2-	pyridin-2,6-diyl	bond	2,5-diMeO-phenyl
270	-CH_2-	pyridin-2,6-diyl	bond	2,6-diMeO-phenyl
271	-CH_2-	pyridin-2,6-diyl	bond	3,4-diMeO-phenyl
272	-CH_2-	pyridin-2,6-diyl	bond	3,5-diMeO-phenyl
273	-CH_2-	pyridin-2,6-diyl	bond	cyclopropyl
274	-CH_2-	pyridin-2,6-diyl	bond	cyclobutyl
275	-CH_2-	pyridin-2,6-diyl	bond	cyclopentyl

276	-CH_2-	pyridin-2,6-diyl	bond	cyclohexyl
277	-CH_2-	pyridin-2,6-diyl	bond	2-furanyl
278	-CH_2-	pyridin-2,6-diyl	bond	2-thienyl
279	-CH_2-	pyridin-2,6-diyl	bond	2-imidazolyl
280	-CH_2-	pyridin-2,6-diyl	bond	2-pyridyl
281	-CH_2-	pyridin-2,6-diyl	bond	3-pyridyl
282	-CH_2-	pyridin-2,6-diyl	bond	4-pyridyl
283	-CH_2-	pyridin-2,6-diyl	bond	N-morpholinyl
284	-CH_2-	pyridin-2,6-diyl	bond	N-piperidinyl
285	-CH_2-	pyridin-2,6-diyl	bond	3-Me-2-pyridyl
286	-CH_2-	pyridin-2,6-diyl	bond	4-Me-2-pyridyl
287	-CH_2-	pyridin-2,6-diyl	bond	1-indolyl
288	-CH_2-	pyridin-2,6-diyl	bond	2-benzothienyl
289	-CH_2-	pyridin-2,6-diyl	bond	2-benzofuranyl
290	-CH_2-	pyridin-2,6-diyl	bond	1-benzimidazole
291	-CH_2-	pyridin-2,6-diyl	bond	2-naphthyl
292	-CH_2-	pyridin-2,4-diyl	bond	phenyl
293	-CH_2-	pyridin-2,4-diyl	bond	3,3-diphenylmethyl
294	-CH_2-	pyridin-2,4-diyl	bond	2-F-phenyl
295	-CH_2-	pyridin-2,4-diyl	bond	3-F-phenyl
296	-CH_2-	pyridin-2,4-diyl	bond	4-F-phenyl
297	-CH_2-	pyridin-2,4-diyl	bond	2-Cl-phenyl
298	-CH_2-	pyridin-2,4-diyl	bond	3-Cl-phenyl
299	-CH_2-	pyridin-2,4-diyl	bond	4-Cl-phenyl
300	-CH_2-	pyridin-2,4-diyl	bond	2-Me-phenyl
301	-CH_2-	pyridin-2,4-diyl	bond	3-Me-phenyl
302	-CH_2-	pyridin-2,4-diyl	bond	4-Me-phenyl
303	-CH_2-	pyridin-2,4-diyl	bond	2-MeO-phenyl
304	-CH_2-	pyridin-2,4-diyl	bond	3-MeO-phenyl
305	-CH_2-	pyridin-2,4-diyl	bond	4-MeO-phenyl
306	-CH_2-	pyridin-2,4-diyl	bond	2-MeS-phenyl
307	-CH_2-	pyridin-2,4-diyl	bond	3-MeS-phenyl
308	-CH_2-	pyridin-2,4-diyl	bond	4-MeS-phenyl
309	-CH_2-	pyridin-2,4-diyl	bond	2-F_3C-phenyl

310	$-CH_2-$	pyridin-2,4-diyl	bond	3-F_3C-phenyl
311	$-CH_2-$	pyridin-2,4-diyl	bond	4-F_3C-phenyl
312	$-CH_2-$	pyridin-2,4-diyl	bond	2,3-diF-phenyl
313	$-CH_2-$	pyridin-2,4-diyl	bond	2,4-diF-phenyl
314	$-CH_2-$	pyridin-2,4-diyl	bond	2,5-diF-phenyl
315	$-CH_2-$	pyridin-2,4-diyl	bond	2,6-diF-phenyl
316	$-CH_2-$	pyridin-2,4-diyl	bond	3,4-diF-phenyl
317	$-CH_2-$	pyridin-2,4-diyl	bond	3,5-diF-phenyl
318	$-CH_2-$	pyridin-2,4-diyl	bond	2,3-diCl-phenyl
319	$-CH_2-$	pyridin-2,4-diyl	bond	2,4-diCl-phenyl
320	$-CH_2-$	pyridin-2,4-diyl	bond	2,5-diCl-phenyl
321	$-CH_2-$	pyridin-2,4-diyl	bond	2,6-diCl-phenyl
322	$-CH_2-$	pyridin-2,4-diyl	bond	3,4-diCl-phenyl
323	$-CH_2-$	pyridin-2,4-diyl	bond	3,5-diCl-phenyl
324	$-CH_2-$	pyridin-2,4-diyl	bond	2-Cl-3-F-phenyl
325	$-CH_2-$	pyridin-2,4-diyl	bond	2-Cl-4-F-phenyl
326	$-CH_2-$	pyridin-2,4-diyl	bond	2-Cl-5-F-phenyl
327	$-CH_2-$	pyridin-2,4-diyl	bond	3-Cl-4-F-phenyl
328	$-CH_2-$	pyridin-2,4-diyl	bond	3-Cl-5-F-phenyl
329	$-CH_2-$	pyridin-2,4-diyl	bond	4-Cl-2-F-phenyl
330	$-CH_2-$	pyridin-2,4-diyl	bond	4-Cl-3-F-phenyl
331	$-CH_2-$	pyridin-2,4-diyl	bond	2,3-diMeO-phenyl
332	$-CH_2-$	pyridin-2,4-diyl	bond	2,4-diMeO-phenyl
333	$-CH_2-$	pyridin-2,4-diyl	bond	2,5-diMeO-phenyl
334	$-CH_2-$	pyridin-2,4-diyl	bond	2,6-diMeO-phenyl
335	$-CH_2-$	pyridin-2,4-diyl	bond	3,4-diMeO-phenyl
336	$-CH_2-$	pyridin-2,4-diyl	bond	3,5-diMeO-phenyl
337	$-CH_2-$	pyridin-2,4-diyl	bond	cyclopropyl
338	$-CH_2-$	pyridin-2,4-diyl	bond	cyclobutyl
339	$-CH_2-$	pyridin-2,4-diyl	bond	cyclopentyl
340	$-CH_2-$	pyridin-2,4-diyl	bond	cyclohexyl
341	$-CH_2-$	pyridin-2,4-diyl	bond	2-furanyl
342	$-CH_2-$	pyridin-2,4-diyl	bond	2-thienyl
343	$-CH_2-$	pyridin-2,4-diyl	bond	2-imidazolyl

344	-CH_2-	pyridin-2,4-diyl	bond	2-pyridyl
345	-CH_2-	pyridin-2,4-diyl	bond	3-pyridyl
346	-CH_2-	pyridin-2,4-diyl	bond	4-pyridyl
347	-CH_2-	pyridin-2,4-diyl	bond	N-morpholinyl
348	-CH_2-	pyridin-2,4-diyl	bond	N-piperidinyl
349	-CH_2-	pyridin-2,4-diyl	bond	3-Me-2-pyridyl
350	-CH_2-	pyridin-2,4-diyl	bond	4-Me-2-pyridyl
351	-CH_2-	pyridin-2,4-diyl	bond	1-indolyl
352	-CH_2-	pyridin-2,4-diyl	bond	2-benzothienyl
353	-CH_2-	pyridin-2,4-diyl	bond	2-benzofuranyl
354	-CH_2-	pyridin-2,4-diyl	bond	1-benzimidazole
355	-CH_2-	pyridin-2,4-diyl	bond	2-naphthyl
356	-CH_2-	pyridin-4,2-diyl	bond	phenyl
357	-CH_2-	pyridin-4,2-diyl	bond	3,3-diphenylmethyl
358	-CH_2-	pyridin-4,2-diyl	bond	2-F-phenyl
359	-CH_2-	pyridin-4,2-diyl	bond	3-F-phenyl
360	-CH_2-	pyridin-4,2-diyl	bond	4-F-phenyl
361	-CH_2-	pyridin-4,2-diyl	bond	2-Cl-phenyl
362	-CH_2-	pyridin-4,2-diyl	bond	3-Cl-phenyl
363	-CH_2-	pyridin-4,2-diyl	bond	4-Cl-phenyl
364	-CH_2-	pyridin-4,2-diyl	bond	2-Me-phenyl
365	-CH_2-	pyridin-4,2-diyl	bond	3-Me-phenyl
366	-CH_2-	pyridin-4,2-diyl	bond	4-Me-phenyl
367	-CH_2-	pyridin-4,2-diyl	bond	2-MeO-phenyl
368	-CH_2-	pyridin-4,2-diyl	bond	3-MeO-phenyl
369	-CH_2-	pyridin-4,2-diyl	bond	4-MeO-phenyl
370	-CH_2-	pyridin-4,2-diyl	bond	2-MeS-phenyl
371	-CH_2-	pyridin-4,2-diyl	bond	3-MeS-phenyl
372	-CH_2-	pyridin-4,2-diyl	bond	4-MeS-phenyl
373	-CH_2-	pyridin-4,2-diyl	bond	2-F_3C-phenyl
374	-CH_2-	pyridin-4,2-diyl	bond	3-F_3C-phenyl
375	-CH_2-	pyridin-4,2-diyl	bond	4-F_3C-phenyl
376	-CH_2-	pyridin-4,2-diyl	bond	2,3-diF-phenyl
377	-CH_2-	pyridin-4,2-diyl	bond	2,4-diF-phenyl

378	-CH_2-	pyridin-4,2-diyl	bond	2,5-diF-phenyl
379	-CH_2-	pyridin-4,2-diyl	bond	2,6-diF-phenyl
380	-CH_2-	pyridin-4,2-diyl	bond	3,4-diF-phenyl
381	-CH_2-	pyridin-4,2-diyl	bond	3,5-diF-phenyl
382	-CH_2-	pyridin-4,2-diyl	bond	2,3-diCl-phenyl
383	-CH_2-	pyridin-4,2-diyl	bond	2,4-diCl-phenyl
384	-CH_2-	pyridin-4,2-diyl	bond	2,5-diCl-phenyl
385	-CH_2-	pyridin-4,2-diyl	bond	2,6-diCl-phenyl
386	-CH_2-	pyridin-4,2-diyl	bond	3,4-diCl-phenyl
387	-CH_2-	pyridin-4,2-diyl	bond	3,5-diCl-phenyl
388	-CH_2-	pyridin-4,2-diyl	bond	2-Cl-3-F-phenyl
389	-CH_2-	pyridin-4,2-diyl	bond	2-Cl-4-F-phenyl
390	-CH_2-	pyridin-4,2-diyl	bond	2-Cl-5-F-phenyl
391	-CH_2-	pyridin-4,2-diyl	bond	3-Cl-4-F-phenyl
392	-CH_2-	pyridin-4,2-diyl	bond	3-Cl-5-F-phenyl
393	-CH_2-	pyridin-4,2-diyl	bond	4-Cl-2-F-phenyl
394	-CH_2-	pyridin-4,2-diyl	bond	4-Cl-3-F-phenyl
395	-CH_2-	pyridin-4,2-diyl	bond	2,3-diMeO-phenyl
396	-CH_2-	pyridin-4,2-diyl	bond	2,4-diMeO-phenyl
397	-CH_2-	pyridin-4,2-diyl	bond	2,5-diMeO-phenyl
398	-CH_2-	pyridin-4,2-diyl	bond	2,6-diMeO-phenyl
399	-CH_2-	pyridin-4,2-diyl	bond	3,4-diMeO-phenyl
400	-CH_2-	pyridin-4,2-diyl	bond	3,5-diMeO-phenyl
401	-CH_2-	pyridin-4,2-diyl	bond	cyclopropyl
402	-CH_2-	pyridin-4,2-diyl	bond	cyclobutyl
403	-CH_2-	pyridin-4,2-diyl	bond	cyclopentyl
404	-CH_2-	pyridin-4,2-diyl	bond	cyclohexyl
405	-CH_2-	pyridin-4,2-diyl	bond	2-furanyl
406	-CH_2-	pyridin-4,2-diyl	bond	2-thienyl
407	-CH_2-	pyridin-4,2-diyl	bond	2-imidazolyl
408	-CH_2-	pyridin-4,2-diyl	bond	2-pyridyl
409	-CH_2-	pyridin-4,2-diyl	bond	3-pyridyl
410	-CH_2-	pyridin-4,2-diyl	bond	4-pyridyl
411	-CH_2-	pyridin-4,2-diyl	bond	N-morpholinyl

412	-CH_2-	pyridin-4,2-diyl	bond	N-piperidinyl
413	-CH_2-	pyridin-4,2-diyl	bond	3-Me-2-pyridyl
414	-CH_2-	pyridin-4,2-diyl	bond	4-Me-2-pyridyl
415	-CH_2-	pyridin-4,2-diyl	bond	1-indolyl
416	-CH_2-	pyridin-4,2-diyl	bond	2-benzothienyl
417	-CH_2-	pyridin-4,2-diyl	bond	2-benzofuranyl
418	-CH_2-	pyridin-4,2-diyl	bond	1-benzimidazole
419	-CH_2-	pyridin-4,2-diyl	bond	2-naphthyl
420	-CH_2-	piperidin-1,3-diyl	bond	phenyl
421	-CH_2-	piperidin-1,3-diyl	bond	3,3-diphenylmethyl
422	-CH_2-	piperidin-1,3-diyl	bond	2-F-phenyl
423	-CH_2-	piperidin-1,3-diyl	bond	3-F-phenyl
424	-CH_2-	piperidin-1,3-diyl	bond	4-F-phenyl
425	-CH_2-	piperidin-1,3-diyl	bond	2-Cl-phenyl
426	-CH_2-	piperidin-1,3-diyl	bond	3-Cl-phenyl
427	-CH_2-	piperidin-1,3-diyl	bond	4-Cl-phenyl
428	-CH_2-	piperidin-1,3-diyl	bond	2-Me-phenyl
429	-CH_2-	piperidin-1,3-diyl	bond	3-Me-phenyl
430	-CH_2-	piperidin-1,3-diyl	bond	4-Me-phenyl
431	-CH_2-	piperidin-1,3-diyl	bond	2-MeO-phenyl
432	-CH_2-	piperidin-1,3-diyl	bond	3-MeO-phenyl
433	-CH_2-	piperidin-1,3-diyl	bond	4-MeO-phenyl
434	-CH_2-	piperidin-1,3-diyl	bond	2-MeS-phenyl
435	-CH_2-	piperidin-1,3-diyl	bond	3-MeS-phenyl
436	-CH_2-	piperidin-1,3-diyl	bond	4-MeS-phenyl
437	-CH_2-	piperidin-1,3-diyl	bond	2-F_3C-phenyl
438	-CH_2-	piperidin-1,3-diyl	bond	3-F_3C-phenyl
439	-CH_2-	piperidin-1,3-diyl	bond	4-F_3C-phenyl
440	-CH_2-	piperidin-1,3-diyl	bond	2,3-diF-phenyl
441	-CH_2-	piperidin-1,3-diyl	bond	2,4-diF-phenyl
442	-CH_2-	piperidin-1,3-diyl	bond	2,5-diF-phenyl
443	-CH_2-	piperidin-1,3-diyl	bond	2,6-diF-phenyl
444	-CH_2-	piperidin-1,3-diyl	bond	3,4-diF-phenyl
445	-CH_2-	piperidin-1,3-diyl	bond	3,5-diF-phenyl

446	$-CH_2-$	piperidin-1,3-diyl	bond	2,3-diCl-phenyl
447	$-CH_2-$	piperidin-1,3-diyl	bond	2,4-diCl-phenyl
448	$-CH_2-$	piperidin-1,3-diyl	bond	2,5-diCl-phenyl
449	$-CH_2-$	piperidin-1,3-diyl	bond	2,6-diCl-phenyl
450	$-CH_2-$	piperidin-1,3-diyl	bond	3,4-diCl-phenyl
451	$-CH_2-$	piperidin-1,3-diyl	bond	3,5-diCl-phenyl
452	$-CH_2-$	piperidin-1,3-diyl	bond	2-Cl-3-F-phenyl
453	$-CH_2-$	piperidin-1,3-diyl	bond	2-Cl-4-F-phenyl
454	$-CH_2-$	piperidin-1,3-diyl	bond	2-Cl-5-F-phenyl
455	$-CH_2-$	piperidin-1,3-diyl	bond	3-Cl-4-F-phenyl
456	$-CH_2-$	piperidin-1,3-diyl	bond	3-Cl-5-F-phenyl
457	$-CH_2-$	piperidin-1,3-diyl	bond	4-Cl-2-F-phenyl
458	$-CH_2-$	piperidin-1,3-diyl	bond	4-Cl-3-F-phenyl
459	$-CH_2-$	piperidin-1,3-diyl	bond	2,3-diMeO-phenyl
460	$-CH_2-$	piperidin-1,3-diyl	bond	2,4-diMeO-phenyl
461	$-CH_2-$	piperidin-1,3-diyl	bond	2,5-diMeO-phenyl
462	$-CH_2-$	piperidin-1,3-diyl	bond	2,6-diMeO-phenyl
463	$-CH_2-$	piperidin-1,3-diyl	bond	3,4-diMeO-phenyl
464	$-CH_2-$	piperidin-1,3-diyl	bond	3,5-diMeO-phenyl
465	$-CH_2-$	piperidin-1,3-diyl	bond	cyclopropyl
466	$-CH_2-$	piperidin-1,3-diyl	bond	cyclobutyl
467	$-CH_2-$	piperidin-1,3-diyl	bond	cyclopentyl
468	$-CH_2-$	piperidin-1,3-diyl	bond	cyclohexyl
469	$-CH_2-$	piperidin-1,3-diyl	bond	2-furanyl
470	$-CH_2-$	piperidin-1,3-diyl	bond	2-thienyl
471	$-CH_2-$	piperidin-1,3-diyl	bond	2-imidazolyl
472	$-CH_2-$	piperidin-1,3-diyl	bond	2-pyridyl
473	$-CH_2-$	piperidin-1,3-diyl	bond	3-pyridyl
474	$-CH_2-$	piperidin-1,3-diyl	bond	4-pyridyl
475	$-CH_2-$	piperidin-1,3-diyl	bond	N-morpholinyl
476	$-CH_2-$	piperidin-1,3-diyl	bond	N-piperidinyl
477	$-CH_2-$	piperidin-1,3-diyl	bond	3-Me-2-pyridyl
478	$-CH_2-$	piperidin-1,3-diyl	bond	4-Me-2-pyridyl
479	$-CH_2-$	piperidin-1,3-diyl	bond	1-indolyl

480	-CH_2-	piperidin-1,3-diyl	bond	2-benzothienyl
481	-CH_2-	piperidin-1,3-diyl	bond	2-benzofuranyl
482	-CH_2-	piperidin-1,3-diyl	bond	1-benzimidazole
483	-CH_2-	piperidin-1,3-diyl	bond	2-naphthyl
484	-CH_2-	piperidin-3,1-diyl	bond	phenyl
485	-CH_2-	piperidin-3,1-diyl	bond	3,3-diphenylmethyl
486	-CH_2-	piperidin-3,1-diyl	bond	2-F-phenyl
487	-CH_2-	piperidin-3,1-diyl	bond	3-F-phenyl
488	-CH_2-	piperidin-3,1-diyl	bond	4-F-phenyl
489	-CH_2-	piperidin-3,1-diyl	bond	2-Cl-phenyl
490	-CH_2-	piperidin-3,1-diyl	bond	3-Cl-phenyl
491	-CH_2-	piperidin-3,1-diyl	bond	4-Cl-phenyl
492	-CH_2-	piperidin-3,1-diyl	bond	2-Me-phenyl
493	-CH_2-	piperidin-3,1-diyl	bond	3-Me-phenyl
494	-CH_2-	piperidin-3,1-diyl	bond	4-Me-phenyl
495	-CH_2-	piperidin-3,1-diyl	bond	2-MeO-phenyl
496	-CH_2-	piperidin-3,1-diyl	bond	3-MeO-phenyl
497	-CH_2-	piperidin-3,1-diyl	bond	4-MeO-phenyl
498	-CH_2-	piperidin-3,1-diyl	bond	2-MeS-phenyl
499	-CH_2-	piperidin-3,1-diyl	bond	3-MeS-phenyl
500	-CH_2-	piperidin-3,1-diyl	bond	4-MeS-phenyl
501	-CH_2-	piperidin-3,1-diyl	bond	2-F_3C-phenyl
502	-CH_2-	piperidin-3,1-diyl	bond	3-F_3C-phenyl
503	-CH_2-	piperidin-3,1-diyl	bond	4-F_3C-phenyl
504	-CH_2-	piperidin-3,1-diyl	bond	2,3-diF-phenyl
505	-CH_2-	piperidin-3,1-diyl	bond	2,4-diF-phenyl
506	-CH_2-	piperidin-3,1-diyl	bond	2,5-diF-phenyl
507	-CH_2-	piperidin-3,1-diyl	bond	2,6-diF-phenyl
508	-CH_2-	piperidin-3,1-diyl	bond	3,4-diF-phenyl
509	-CH_2-	piperidin-3,1-diyl	bond	3,5-diF-phenyl
510	-CH_2-	piperidin-3,1-diyl	bond	2,3-diCl-phenyl
511	-CH_2-	piperidin-3,1-diyl	bond	2,4-diCl-phenyl
512	-CH_2-	piperidin-3,1-diyl	bond	2,5-diCl-phenyl
513	-CH_2-	piperidin-3,1-diyl	bond	2,6-diCl-phenyl

514	-CH_2-	piperidin-3,1-diyl	bond	3,4-diCl-phenyl
515	-CH_2-	piperidin-3,1-diyl	bond	3,5-diCl-phenyl
516	-CH_2-	piperidin-3,1-diyl	bond	2-Cl-3-F-phenyl
517	-CH_2-	piperidin-3,1-diyl	bond	2-Cl-4-F-phenyl
518	-CH_2-	piperidin-3,1-diyl	bond	2-Cl-5-F-phenyl
519	-CH_2-	piperidin-3,1-diyl	bond	3-Cl-4-F-phenyl
520	-CH_2-	piperidin-3,1-diyl	bond	3-Cl-5-F-phenyl
521	-CH_2-	piperidin-3,1-diyl	bond	4-Cl-2-F-phenyl
522	-CH_2-	piperidin-3,1-diyl	bond	4-Cl-3-F-phenyl
523	-CH_2-	piperidin-3,1-diyl	bond	2,3-diMeO-phenyl
524	-CH_2-	piperidin-3,1-diyl	bond	2,4-diMeO-phenyl
525	-CH_2-	piperidin-3,1-diyl	bond	2,5-diMeO-phenyl
526	-CH_2-	piperidin-3,1-diyl	bond	2,6-diMeO-phenyl
527	-CH_2-	piperidin-3,1-diyl	bond	3,4-diMeO-phenyl
528	-CH_2-	piperidin-3,1-diyl	bond	3,5-diMeO-phenyl
529	-CH_2-	piperidin-3,1-diyl	bond	cyclopropyl
530	-CH_2-	piperidin-3,1-diyl	bond	cyclobutyl
531	-CH_2-	piperidin-3,1-diyl	bond	cyclopentyl
532	-CH_2-	piperidin-3,1-diyl	bond	cyclohexyl
533	-CH_2-	piperidin-3,1-diyl	bond	2-furanyl
534	-CH_2-	piperidin-3,1-diyl	bond	2-thienyl
535	-CH_2-	piperidin-3,1-diyl	bond	2-imidazolyl
536	-CH_2-	piperidin-3,1-diyl	bond	2-pyridyl
537	-CH_2-	piperidin-3,1-diyl	bond	3-pyridyl
538	-CH_2-	piperidin-3,1-diyl	bond	4-pyridyl
539	-CH_2-	piperidin-3,1-diyl	bond	N-morpholinyl
540	-CH_2-	piperidin-3,1-diyl	bond	N-piperidinyl
541	-CH_2-	piperidin-3,1-diyl	bond	3-Me-2-pyridyl
542	-CH_2-	piperidin-3,1-diyl	bond	4-Me-2-pyridyl
543	-CH_2-	piperidin-3,1-diyl	bond	1-indolyl
544	-CH_2-	piperidin-3,1-diyl	bond	2-benzothienyl
545	-CH_2-	piperidin-3,1-diyl	bond	2-benzofuranyl
546	-CH_2-	piperidin-3,1-diyl	bond	1-benzimidazole
547	-CH_2-	piperidin-3,1-diyl	bond	2-naphthyl

548	-CH_2-	cyclohex-1,3-diyl	bond	phenyl
549	-CH_2-	cyclohex-1,3-diyl	bond	3,3-diphenylmethyl
550	-CH_2-	cyclohex-1,3-diyl	bond	2-F-phenyl
551	-CH_2-	cyclohex-1,3-diyl	bond	3-F-phenyl
552	-CH_2-	cyclohex-1,3-diyl	bond	4-F-phenyl
553	-CH_2-	cyclohex-1,3-diyl	bond	2-Cl-phenyl
554	-CH_2-	cyclohex-1,3-diyl	bond	3-Cl-phenyl
555	-CH_2-	cyclohex-1,3-diyl	bond	4-Cl-phenyl
556	-CH_2-	cyclohex-1,3-diyl	bond	2-Me-phenyl
557	-CH_2-	cyclohex-1,3-diyl	bond	3-Me-phenyl
558	-CH_2-	cyclohex-1,3-diyl	bond	4-Me-phenyl
559	-CH_2-	cyclohex-1,3-diyl	bond	2-MeO-phenyl
560	-CH_2-	cyclohex-1,3-diyl	bond	3-MeO-phenyl
561	-CH_2-	cyclohex-1,3-diyl	bond	4-MeO-phenyl
562	-CH_2-	cyclohex-1,3-diyl	bond	2-MeS-phenyl
563	-CH_2-	cyclohex-1,3-diyl	bond	3-MeS-phenyl
564	-CH_2-	cyclohex-1,3-diyl	bond	4-MeS-phenyl
565	-CH_2-	cyclohex-1,3-diyl	bond	2-F_3C-phenyl
566	-CH_2-	cyclohex-1,3-diyl	bond	3-F_3C-phenyl
567	-CH_2-	cyclohex-1,3-diyl	bond	4-F_3C-phenyl
568	-CH_2-	cyclohex-1,3-diyl	bond	2,3-diF-phenyl
569	-CH_2-	cyclohex-1,3-diyl	bond	2,4-diF-phenyl
570	-CH_2-	cyclohex-1,3-diyl	bond	2,5-diF-phenyl
571	-CH_2-	cyclohex-1,3-diyl	bond	2,6-diF-phenyl
572	-CH_2-	cyclohex-1,3-diyl	bond	3,4-diF-phenyl
573	-CH_2-	cyclohex-1,3-diyl	bond	3,5-diF-phenyl
574	-CH_2-	cyclohex-1,3-diyl	bond	2,3-diCl-phenyl
575	-CH_2-	cyclohex-1,3-diyl	bond	2,4-diCl-phenyl
576	-CH_2-	cyclohex-1,3-diyl	bond	2,5-diCl-phenyl
577	-CH_2-	cyclohex-1,3-diyl	bond	2,6-diCl-phenyl
578	-CH_2-	cyclohex-1,3-diyl	bond	3,4-diCl-phenyl
579	-CH_2-	cyclohex-1,3-diyl	bond	3,5-diCl-phenyl
580	-CH_2-	cyclohex-1,3-diyl	bond	2-Cl-3-F-phenyl
581	-CH_2-	cyclohex-1,3-diyl	bond	2-Cl-4-F-phenyl

582	-CH_2-	cyclohex-1,3-diyl	bond	2-Cl-5-F-phenyl
583	-CH_2-	cyclohex-1,3-diyl	bond	3-Cl-4-F-phenyl
584	-CH_2-	cyclohex-1,3-diyl	bond	3-Cl-5-F-phenyl
585	-CH_2-	cyclohex-1,3-diyl	bond	4-Cl-2-F-phenyl
586	-CH_2-	cyclohex-1,3-diyl	bond	4-Cl-3-F-phenyl
587	-CH_2-	cyclohex-1,3-diyl	bond	2,3-diMeO-phenyl
588	-CH_2-	cyclohex-1,3-diyl	bond	2,4-diMeO-phenyl
589	-CH_2-	cyclohex-1,3-diyl	bond	2,5-diMeO-phenyl
590	-CH_2-	cyclohex-1,3-diyl	bond	2,6-diMeO-phenyl
591	-CH_2-	cyclohex-1,3-diyl	bond	3,4-diMeO-phenyl
592	-CH_2-	cyclohex-1,3-diyl	bond	3,5-diMeO-phenyl
593	-CH_2-	cyclohex-1,3-diyl	bond	cyclopropyl
594	-CH_2-	cyclohex-1,3-diyl	bond	cyclobutyl
595	-CH_2-	cyclohex-1,3-diyl	bond	cyclopentyl
596	-CH_2-	cyclohex-1,3-diyl	bond	cyclohexyl
597	-CH_2-	cyclohex-1,3-diyl	bond	2-furanyl
598	-CH_2-	cyclohex-1,3-diyl	bond	2-thienyl
599	-CH_2-	cyclohex-1,3-diyl	bond	2-imidazolyl
600	-CH_2-	cyclohex-1,3-diyl	bond	2-pyridyl
601	-CH_2-	cyclohex-1,3-diyl	bond	3-pyridyl
602	-CH_2-	cyclohex-1,3-diyl	bond	4-pyridyl
603	-CH_2-	cyclohex-1,3-diyl	bond	N-morpholinyl
604	-CH_2-	cyclohex-1,3-diyl	bond	N-piperidinyl
605	-CH_2-	cyclohex-1,3-diyl	bond	3-Me-2-pyridyl
606	-CH_2-	cyclohex-1,3-diyl	bond	4-Me-2-pyridyl
607	-CH_2-	cyclohex-1,3-diyl	bond	1-indolyl
608	-CH_2-	cyclohex-1,3-diyl	bond	2-benzothienyl
609	-CH_2-	cyclohex-1,3-diyl	bond	2-benzofuranyl
610	-CH_2-	cyclohex-1,3-diyl	bond	1-benzimidazole
611	-CH_2-	cyclohex-1,3-diyl	bond	2-naphthyl
612	-CH_2-	cyclopropan-1,2-diyl	bond	phenyl
613	-CH_2-	cyclopropan-1,2-diyl	bond	3,3-diphenylmethyl
614	-CH_2-	cyclopropan-1,2-diyl	bond	2-F-phenyl
615	-CH_2-	cyclopropan-1,2-diyl	bond	3-F-phenyl

616	$-CH_2-$	cyclopropan-1,2-diyl	bond	4-F-phenyl
617	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-Cl-phenyl
618	$-CH_2-$	cyclopropan-1,2-diyl	bond	3-Cl-phenyl
619	$-CH_2-$	cyclopropan-1,2-diyl	bond	4-Cl-phenyl
620	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-Me-phenyl
621	$-CH_2-$	cyclopropan-1,2-diyl	bond	3-Me-phenyl
622	$-CH_2-$	cyclopropan-1,2-diyl	bond	4-Me-phenyl
623	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-MeO-phenyl
624	$-CH_2-$	cyclopropan-1,2-diyl	bond	3-MeO-phenyl
625	$-CH_2-$	cyclopropan-1,2-diyl	bond	4-MeO-phenyl
626	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-MeS-phenyl
627	$-CH_2-$	cyclopropan-1,2-diyl	bond	3-MeS-phenyl
628	$-CH_2-$	cyclopropan-1,2-diyl	bond	4-MeS-phenyl
629	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-F_3C-phenyl
630	$-CH_2-$	cyclopropan-1,2-diyl	bond	3-F_3C-phenyl
631	$-CH_2-$	cyclopropan-1,2-diyl	bond	4-F_3C-phenyl
632	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,3-diF-phenyl
633	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,4-diF-phenyl
634	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,5-diF-phenyl
635	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,6-diF-phenyl
636	$-CH_2-$	cyclopropan-1,2-diyl	bond	3,4-diF-phenyl
637	$-CH_2-$	cyclopropan-1,2-diyl	bond	3,5-diF-phenyl
638	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,3-diCl-phenyl
639	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,4-diCl-phenyl
640	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,5-diCl-phenyl
641	$-CH_2-$	cyclopropan-1,2-diyl	bond	2,6-diCl-phenyl
642	$-CH_2-$	cyclopropan-1,2-diyl	bond	3,4-diCl-phenyl
643	$-CH_2-$	cyclopropan-1,2-diyl	bond	3,5-diCl-phenyl
644	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-Cl-3-F-phenyl
645	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-Cl-4-F-phenyl
646	$-CH_2-$	cyclopropan-1,2-diyl	bond	2-Cl-5-F-phenyl
647	$-CH_2-$	cyclopropan-1,2-diyl	bond	3-Cl-4-F-phenyl
648	$-CH_2-$	cyclopropan-1,2-diyl	bond	3-Cl-5-F-phenyl
649	$-CH_2-$	cyclopropan-1,2-diyl	bond	4-Cl-2-F-phenyl

650	-CH_2-	cyclopropan-1,2-diyl	bond	4-Cl-3-F-phenyl
651	-CH_2-	cyclopropan-1,2-diyl	bond	2,3-diMeO-phenyl
652	-CH_2-	cyclopropan-1,2-diyl	bond	2,4-diMeO-phenyl
653	-CH_2-	cyclopropan-1,2-diyl	bond	2,5-diMeO-phenyl
654	-CH_2-	cyclopropan-1,2-diyl	bond	2,6-diMeO-phenyl
655	-CH_2-	cyclopropan-1,2-diyl	bond	3,4-diMeO-phenyl
656	-CH_2-	cyclopropan-1,2-diyl	bond	3,5-diMeO-phenyl
657	-CH_2-	cyclopropan-1,2-diyl	bond	cyclopropyl
658	-CH_2-	cyclopropan-1,2-diyl	bond	cyclobutyl
659	-CH_2-	cyclopropan-1,2-diyl	bond	cyclopentyl
660	-CH_2-	cyclopropan-1,2-diyl	bond	cyclohexyl
661	-CH_2-	cyclopropan-1,2-diyl	bond	2-furanyl
662	-CH_2-	cyclopropan-1,2-diyl	bond	2-thienyl
663	-CH_2-	cyclopropan-1,2-diyl	bond	2-imidazolyl
664	-CH_2-	cyclopropan-1,2-diyl	bond	2-pyridyl
665	-CH_2-	cyclopropan-1,2-diyl	bond	3-pyridyl
666	-CH_2-	cyclopropan-1,2-diyl	bond	4-pyridyl
667	-CH_2-	cyclopropan-1,2-diyl	bond	N-morpholinyl
668	-CH_2-	cyclopropan-1,2-diyl	bond	N-piperidinyl
669	-CH_2-	cyclopropan-1,2-diyl	bond	3-Me-2-pyridyl
670	-CH_2-	cyclopropan-1,2-diyl	bond	4-Me-2-pyridyl
671	-CH_2-	cyclopropan-1,2-diyl	bond	1-indolyl
672	-CH_2-	cyclopropan-1,2-diyl	bond	2-benzothienyl
673	-CH_2-	cyclopropan-1,2-diyl	bond	2-benzofuranyl
674	-CH_2-	cyclopropan-1,2-diyl	bond	1-benzimidazole
675	-CH_2-	cyclopropan-1,2-diyl	bond	2-naphthyl
676	-CH_2-	cyclopentan-1,3-diyl	bond	phenyl
677	-CH_2-	cyclopentan-1,3-diyl	bond	3,3-diphenylmethyl
678	-CH_2-	cyclopentan-1,3-diyl	bond	2-F-phenyl
679	-CH_2-	cyclopentan-1,3-diyl	bond	3-F-phenyl
680	-CH_2-	cyclopentan-1,3-diyl	bond	4-F-phenyl
681	-CH_2-	cyclopentan-1,3-diyl	bond	2-Cl-phenyl
682	-CH_2-	cyclopentan-1,3-diyl	bond	3-Cl-phenyl
683	-CH_2-	cyclopentan-1,3-diyl	bond	4-Cl-phenyl

684	-CH_2-	cyclopentan-1,3-diyl	bond	2-Me-phenyl
685	-CH_2-	cyclopentan-1,3-diyl	bond	3-Me-phenyl
686	-CH_2-	cyclopentan-1,3-diyl	bond	4-Me-phenyl
687	-CH_2-	cyclopentan-1,3-diyl	bond	2-MeO-phenyl
688	-CH_2-	cyclopentan-1,3-diyl	bond	3-MeO-phenyl
689	-CH_2-	cyclopentan-1,3-diyl	bond	4-MeO-phenyl
690	-CH_2-	cyclopentan-1,3-diyl	bond	2-MeS-phenyl
691	-CH_2-	cyclopentan-1,3-diyl	bond	3-MeS-phenyl
692	-CH_2-	cyclopentan-1,3-diyl	bond	4-MeS-phenyl
693	-CH_2-	cyclopentan-1,3-diyl	bond	2-F_3C-phenyl
694	-CH_2-	cyclopentan-1,3-diyl	bond	3-F_3C-phenyl
695	-CH_2-	cyclopentan-1,3-diyl	bond	4-F_3C-phenyl
696	-CH_2-	cyclopentan-1,3-diyl	bond	2,3-diF-phenyl
697	-CH_2-	cyclopentan-1,3-diyl	bond	2,4-diF-phenyl
698	-CH_2-	cyclopentan-1,3-diyl	bond	2,5-diF-phenyl
699	-CH_2-	cyclopentan-1,3-diyl	bond	2,6-diF-phenyl
700	-CH_2-	cyclopentan-1,3-diyl	bond	3,4-diF-phenyl
701	-CH_2-	cyclopentan-1,3-diyl	bond	3,5-diF-phenyl
702	-CH_2-	cyclopentan-1,3-diyl	bond	2,3-diCl-phenyl
703	-CH_2-	cyclopentan-1,3-diyl	bond	2,4-diCl-phenyl
704	-CH_2-	cyclopentan-1,3-diyl	bond	2,5-diCl-phenyl
705	-CH_2-	cyclopentan-1,3-diyl	bond	2,6-diCl-phenyl
706	-CH_2-	cyclopentan-1,3-diyl	bond	3,4-diCl-phenyl
707	-CH_2-	cyclopentan-1,3-diyl	bond	3,5-diCl-phenyl
708	-CH_2-	cyclopentan-1,3-diyl	bond	2-Cl-3-F-phenyl
709	-CH_2-	cyclopentan-1,3-diyl	bond	2-Cl-4-F-phenyl
710	-CH_2-	cyclopentan-1,3-diyl	bond	2-Cl-5-F-phenyl
711	-CH_2-	cyclopentan-1,3-diyl	bond	3-Cl-4-F-phenyl
712	-CH_2-	cyclopentan-1,3-diyl	bond	3-Cl-5-F-phenyl
713	-CH_2-	cyclopentan-1,3-diyl	bond	4-Cl-2-F-phenyl
714	-CH_2-	cyclopentan-1,3-diyl	bond	4-Cl-3-F-phenyl
715	-CH_2-	cyclopentan-1,3-diyl	bond	2,3-diMeO-phenyl
716	-CH_2-	cyclopentan-1,3-diyl	bond	2,4-diMeO-phenyl
717	-CH_2-	cyclopentan-1,3-diyl	bond	2,5-diMeO-phenyl

718	-CH_2-	cyclopentan-1,3-diyl	bond	2,6-diMeO-phenyl
719	-CH_2-	cyclopentan-1,3-diyl	bond	3,4-diMeO-phenyl
720	-CH_2-	cyclopentan-1,3-diyl	bond	3,5-diMeO-phenyl
721	-CH_2-	cyclopentan-1,3-diyl	bond	cyclopropyl
722	-CH_2-	cyclopentan-1,3-diyl	bond	cyclobutyl
723	-CH_2-	cyclopentan-1,3-diyl	bond	cyclopentyl
724	-CH_2-	cyclopentan-1,3-diyl	bond	cyclohexyl
725	-CH_2-	cyclopentan-1,3-diyl	bond	2-furanyl
726	-CH_2-	cyclopentan-1,3-diyl	bond	2-thienyl
727	-CH_2-	cyclopentan-1,3-diyl	bond	2-imidazolyl
728	-CH_2-	cyclopentan-1,3-diyl	bond	2-pyridyl
729	-CH_2-	cyclopentan-1,3-diyl	bond	3-pyridyl
730	-CH_2-	cyclopentan-1,3-diyl	bond	4-pyridyl
731	-CH_2-	cyclopentan-1,3-diyl	bond	N-morpholinyl
732	-CH_2-	cyclopentan-1,3-diyl	bond	N-piperidinyl
733	-CH_2-	cyclopentan-1,3-diyl	bond	3-Me-2-pyridyl
734	-CH_2-	cyclopentan-1,3-diyl	bond	4-Me-2-pyridyl
735	-CH_2-	cyclopentan-1,3-diyl	bond	1-indolyl
736	-CH_2-	cyclopentan-1,3-diyl	bond	2-benzothienyl
737	-CH_2-	cyclopentan-1,3-diyl	bond	2-benzofuranyl
738	-CH_2-	cyclopentan-1,3-diyl	bond	1-benzimidazole
739	-CH_2-	cyclopentan-1,3-diyl	bond	2-naphthyl

740	-CH_2-	phen-1,3-diyl	-O-	phenyl
741	-CH_2-	phen-1,3-diyl	-O-	3,3-diphenylmethyl
742	-CH_2-	phen-1,3-diyl	-O-	2-F-phenyl
743	-CH_2-	phen-1,3-diyl	-O-	3-F-phenyl
744	-CH_2-	phen-1,3-diyl	-O-	4-F-phenyl
745	-CH_2-	phen-1,3-diyl	-O-	2-Cl-phenyl
746	-CH_2-	phen-1,3-diyl	-O-	3-Cl-phenyl
747	-CH_2-	phen-1,3-diyl	-O-	4-Cl-phenyl
748	-CH_2-	phen-1,3-diyl	-O-	2-Me-phenyl
749	-CH_2-	phen-1,3-diyl	-O-	3-Me-phenyl
750	-CH_2-	phen-1,3-diyl	-O-	4-Me-phenyl

751	-CH_2-	phen-1,3-diyl	-O-	2-MeO-phenyl
752	-CH_2-	phen-1,3-diyl	-O-	3-MeO-phenyl
753	-CH_2-	phen-1,3-diyl	-O-	4-MeO-phenyl
754	-CH_2-	phen-1,3-diyl	-O-	2-MeS-phenyl
755	-CH_2-	phen-1,3-diyl	-O-	3-MeS-phenyl
756	-CH_2-	phen-1,3-diyl	-O-	4-MeS-phenyl
757	-CH_2-	phen-1,3-diyl	-O-	2-F_3C-phenyl
758	-CH_2-	phen-1,3-diyl	-O-	3-F_3C-phenyl
759	-CH_2-	phen-1,3-diyl	-O-	4-F_3C-phenyl
760	-CH_2-	phen-1,3-diyl	-O-	2,3-diF-phenyl
761	-CH_2-	phen-1,3-diyl	-O-	2,4-diF-phenyl
762	-CH_2-	phen-1,3-diyl	-O-	2,5-diF-phenyl
763	-CH_2-	phen-1,3-diyl	-O-	2,6-diF-phenyl
764	-CH_2-	phen-1,3-diyl	-O-	3,4-diF-phenyl
765	-CH_2-	phen-1,3-diyl	-O-	3,5-diF-phenyl
766	-CH_2-	phen-1,3-diyl	-O-	2,3-diCl-phenyl
767	-CH_2-	phen-1,3-diyl	-O-	2,4-diCl-phenyl
768	-CH_2-	phen-1,3-diyl	-O-	2,5-diCl-phenyl
769	-CH_2-	phen-1,3-diyl	-O-	2,6-diCl-phenyl
770	-CH_2-	phen-1,3-diyl	-O-	3,4-diCl-phenyl
771	-CH_2-	phen-1,3-diyl	-O-	3,5-diCl-phenyl
772	-CH_2-	phen-1,3-diyl	-O-	2-Cl-3-F-phenyl
773	-CH_2-	phen-1,3-diyl	-O-	2-Cl-4-F-phenyl
774	-CH_2-	phen-1,3-diyl	-O-	2-Cl-5-F-phenyl
775	-CH_2-	phen-1,3-diyl	-O-	3-Cl-4-F-phenyl
776	-CH_2-	phen-1,3-diyl	-O-	3-Cl-5-F-phenyl
777	-CH_2-	phen-1,3-diyl	-O-	4-Cl-2-F-phenyl
778	-CH_2-	phen-1,3-diyl	-O-	4-Cl-3-F-phenyl
779	-CH_2-	phen-1,3-diyl	-O-	2,3-diMeO-phenyl
780	-CH_2-	phen-1,3-diyl	-O-	2,4-diMeO-phenyl
781	-CH_2-	phen-1,3-diyl	-O-	2,5-diMeO-phenyl
782	-CH_2-	phen-1,3-diyl	-O-	2,6-diMeO-phenyl
783	-CH_2-	phen-1,3-diyl	-O-	3,4-diMeO-phenyl
784	-CH_2-	phen-1,3-diyl	-O-	3,5-diMeO-phenyl

785	-CH_2-	phen-1,3-diyl	-O-	cyclopropyl
786	-CH_2-	phen-1,3-diyl	-O-	cyclobutyl
787	-CH_2-	phen-1,3-diyl	-O-	cyclopentyl
788	-CH_2-	phen-1,3-diyl	-O-	cyclohexyl
789	-CH_2-	phen-1,3-diyl	-O-	2-furanyl
790	-CH_2-	phen-1,3-diyl	-O-	2-thienyl
791	-CH_2-	phen-1,3-diyl	CH_2CH_2	2-imidazolyl
792	-CH_2-	phen-1,3-diyl	-O-	2-pyridyl
793	-CH_2-	phen-1,3-diyl	-O-	3-pyridyl
794	-CH_2-	phen-1,3-diyl	-O-	4-pyridyl
795	-CH_2-	phen-1,3-diyl	CH_2CH_2	N-morpholinyl
796	-CH_2-	phen-1,3-diyl	CH_2CH_2	N-piperidinyl
797	-CH_2-	phen-1,3-diyl	-O-	3-Me-2-pyridyl
798	-CH_2-	phen-1,3-diyl	-O-	4-Me-2-pyridyl
799	-CH_2-	phen-1,3-diyl	CH_2CH_2	1-indolyl
800	-CH_2-	phen-1,3-diyl	-O-	2-benzothienyl
801	-CH_2-	phen-1,3-diyl	-O-	2-benzofuranyl
802	-CH_2-	phen-1,3-diyl	CH_2CH_2	1-benzimidazole
803	-CH_2-	phen-1,3-diyl	-O-	2-naphthyl
804	-CH_2-	pyridin-3,5-diyl	-O-	phenyl
805	-CH_2-	pyridin-3,5-diyl	-O-	3,3-diphenylmethyl
806	-CH_2-	pyridin-3,5-diyl	-O-	2-F-phenyl
807	-CH_2-	pyridin-3,5-diyl	-O-	3-F-phenyl
808	-CH_2-	pyridin-3,5-diyl	-O-	4-F-phenyl
809	-CH_2-	pyridin-3,5-diyl	-O-	2-Cl-phenyl
810	-CH_2-	pyridin-3,5-diyl	-O-	3-Cl-phenyl
811	-CH_2-	pyridin-3,5-diyl	-O-	4-Cl-phenyl
812	-CH_2-	pyridin-3,5-diyl	-O-	2-Me-phenyl
813	-CH_2-	pyridin-3,5-diyl	-O-	3-Me-phenyl
814	-CH_2-	pyridin-3,5-diyl	-O-	4-Me-phenyl
815	-CH_2-	pyridin-3,5-diyl	-O-	2-MeO-phenyl
816	-CH_2-	pyridin-3,5-diyl	-O-	3-MeO-phenyl
817	-CH_2-	pyridin-3,5-diyl	-O-	4-MeO-phenyl
818	-CH_2-	pyridin-3,5-diyl	-O-	2-MeS-phenyl

819	-CH_2-	pyridin-3,5-diyl	-O-	3-MeS-phenyl
820	-CH_2-	pyridin-3,5-diyl	-O-	4-MeS-phenyl
821	-CH_2-	pyridin-3,5-diyl	-O-	2-F_3C-phenyl
822	-CH_2-	pyridin-3,5-diyl	-O-	3-F_3C-phenyl
823	-CH_2-	pyridin-3,5-diyl	-O-	4-F_3C-phenyl
824	-CH_2-	pyridin-3,5-diyl	-O-	2,3-diF-phenyl
825	-CH_2-	pyridin-3,5-diyl	-O-	2,4-diF-phenyl
826	-CH_2-	pyridin-3,5-diyl	-O-	2,5-diF-phenyl
827	-CH_2-	pyridin-3,5-diyl	-O-	2,6-diF-phenyl
828	-CH_2-	pyridin-3,5-diyl	-O-	3,4-diF-phenyl
829	-CH_2-	pyridin-3,5-diyl	-O-	3,5-diF-phenyl
830	-CH_2-	pyridin-3,5-diyl	-O-	2,3-diCl-phenyl
831	-CH_2-	pyridin-3,5-diyl	-O-	2,4-diCl-phenyl
832	-CH_2-	pyridin-3,5-diyl	-O-	2,5-diCl-phenyl
833	-CH_2-	pyridin-3,5-diyl	-O-	2,6-diCl-phenyl
834	-CH_2-	pyridin-3,5-diyl	-O-	3,4-diCl-phenyl
835	-CH_2-	pyridin-3,5-diyl	-O-	3,5-diCl-phenyl
836	-CH_2-	pyridin-3,5-diyl	-O-	2-Cl-3-F-phenyl
837	-CH_2-	pyridin-3,5-diyl	-O-	2-Cl-4-F-phenyl
838	-CH_2-	pyridin-3,5-diyl	-O-	2-Cl-5-F-phenyl
839	-CH_2-	pyridin-3,5-diyl	-O-	3-Cl-4-F-phenyl
840	-CH_2-	pyridin-3,5-diyl	-O-	3-Cl-5-F-phenyl
841	-CH_2-	pyridin-3,5-diyl	-O-	4-Cl-2-F-phenyl
842	-CH_2-	pyridin-3,5-diyl	-O-	4-Cl-3-F-phenyl
843	-CH_2-	pyridin-3,5-diyl	-O-	2,3-diMeO-phenyl
844	-CH_2-	pyridin-3,5-diyl	-O-	2,4-diMeO-phenyl
845	-CH_2-	pyridin-3,5-diyl	-O-	2,5-diMeO-phenyl
846	-CH_2-	pyridin-3,5-diyl	-O-	2,6-diMeO-phenyl
847	-CH_2-	pyridin-3,5-diyl	-O-	3,4-diMeO-phenyl
848	-CH_2-	pyridin-3,5-diyl	-O-	3,5-diMeO-phenyl
849	-CH_2-	pyridin-3,5-diyl	-O-	cyclopropyl
850	-CH_2-	pyridin-3,5-diyl	-O-	cyclobutyl
851	-CH_2-	pyridin-3,5-diyl	-O-	cyclopentyl
852	-CH_2-	pyridin-3,5-diyl	-O-	cyclohexyl

853	-CH_2-	pyridin-3,5-diyl	-O-	2-furanyl
854	-CH_2-	pyridin-3,5-diyl	-O-	2-thienyl
855	-CH_2-	pyridin-3,5-diyl	CH_2CH_2	2-imidazolyl
856	-CH_2-	pyridin-3,5-diyl	-O-	2-pyridyl
857	-CH_2-	pyridin-3,5-diyl	-O-	3-pyridyl
858	-CH_2-	pyridin-3,5-diyl	-O-	4-pyridyl
859	-CH_2-	pyridin-3,5-diyl	CH_2CH_2	N-morpholinyl
860	-CH_2-	pyridin-3,5-diyl	CH_2CH_2	N-piperidinyl
861	-CH_2-	pyridin-3,5-diyl	-O-	3-Me-2-pyridyl
862	-CH_2-	pyridin-3,5-diyl	-O-	4-Me-2-pyridyl
863	-CH_2-	pyridin-3,5-diyl	CH_2CH_2	1-indolyl
864	-CH_2-	pyridin-3,5-diyl	-O-	2-benzothienyl
865	-CH_2-	pyridin-3,5-diyl	-O-	2-benzofuranyl
866	-CH_2-	pyridin-3,5-diyl	CH_2CH_2	1-benzimidazole
867	-CH_2-	pyridin-3,5-diyl	-O-	2-naphthyl
868	-CH_2-	pyridin-2,6-diyl	-O-	phenyl
869	-CH_2-	pyridin-2,6-diyl	-O-	3,3-diphenylmethyl
870	-CH_2-	pyridin-2,6-diyl	-O-	2-F-phenyl
871	-CH_2-	pyridin-2,6-diyl	-O-	3-F-phenyl
872	-CH_2-	pyridin-2,6-diyl	-O-	4-F-phenyl
873	-CH_2-	pyridin-2,6-diyl	-O-	2-Cl-phenyl
874	-CH_2-	pyridin-2,6-diyl	-O-	3-Cl-phenyl
875	-CH_2-	pyridin-2,6-diyl	-O-	4-Cl-phenyl
876	-CH_2-	pyridin-2,6-diyl	-O-	2-Me-phenyl
877	-CH_2-	pyridin-2,6-diyl	-O-	3-Me-phenyl
878	-CH_2-	pyridin-2,6-diyl	-O-	4-Me-phenyl
879	-CH_2-	pyridin-2,6-diyl	-O-	2-MeO-phenyl
880	-CH_2-	pyridin-2,6-diyl	-O-	3-MeO-phenyl
881	-CH_2-	pyridin-2,6-diyl	-O-	4-MeO-phenyl
882	-CH_2-	pyridin-2,6-diyl	-O-	2-MeS-phenyl
883	-CH_2-	pyridin-2,6-diyl	-O-	3-MeS-phenyl
884	-CH_2-	pyridin-2,6-diyl	-O-	4-MeS-phenyl
885	-CH_2-	pyridin-2,6-diyl	-O-	2-F_3C-phenyl
886	-CH_2-	pyridin-2,6-diyl	-O-	3-F_3C-phenyl

887	-CH_2-	pyridin-2,6-diyl	-O-	4-F_3C-phenyl
888	-CH_2-	pyridin-2,6-diyl	-O-	2,3-diF-phenyl
889	-CH_2-	pyridin-2,6-diyl	-O-	2,4-diF-phenyl
890	-CH_2-	pyridin-2,6-diyl	-O-	2,5-diF-phenyl
891	-CH_2-	pyridin-2,6-diyl	-O-	2,6-diF-phenyl
892	-CH_2-	pyridin-2,6-diyl	-O-	3,4-diF-phenyl
893	-CH_2-	pyridin-2,6-diyl	-O-	3,5-diF-phenyl
894	-CH_2-	pyridin-2,6-diyl	-O-	2,3-diCl-phenyl
895	-CH_2-	pyridin-2,6-diyl	-O-	2,4-diCl-phenyl
896	-CH_2-	pyridin-2,6-diyl	-O-	2,5-diCl-phenyl
897	-CH_2-	pyridin-2,6-diyl	-O-	2,6-diCl-phenyl
898	-CH_2-	pyridin-2,6-diyl	-O-	3,4-diCl-phenyl
899	-CH_2-	pyridin-2,6-diyl	-O-	3,5-diCl-phenyl
900	-CH_2-	pyridin-2,6-diyl	-O-	2-Cl-3-F-phenyl
901	-CH_2-	pyridin-2,6-diyl	-O-	2-Cl-4-F-phenyl
902	-CH_2-	pyridin-2,6-diyl	-O-	2-Cl-5-F-phenyl
903	-CH_2-	pyridin-2,6-diyl	-O-	3-Cl-4-F-phenyl
904	-CH_2-	pyridin-2,6-diyl	-O-	3-Cl-5-F-phenyl
905	-CH_2-	pyridin-2,6-diyl	-O-	4-Cl-2-F-phenyl
906	-CH_2-	pyridin-2,6-diyl	-O-	4-Cl-3-F-phenyl
907	-CH_2-	pyridin-2,6-diyl	-O-	2,3-diMeO-phenyl
908	-CH_2-	pyridin-2,6-diyl	-O-	2,4-diMeO-phenyl
909	-CH_2-	pyridin-2,6-diyl	-O-	2,5-diMeO-phenyl
910	-CH_2-	pyridin-2,6-diyl	-O-	2,6-diMeO-phenyl
911	-CH_2-	pyridin-2,6-diyl	-O-	3,4-diMeO-phenyl
912	-CH_2-	pyridin-2,6-diyl	-O-	3,5-diMeO-phenyl
913	-CH_2-	pyridin-2,6-diyl	-O-	cyclopropyl
914	-CH_2-	pyridin-2,6-diyl	-O-	cyclobutyl
915	-CH_2-	pyridin-2,6-diyl	-O-	cyclopentyl
916	-CH_2-	pyridin-2,6-diyl	-O-	cyclohexyl
917	-CH_2-	pyridin-2,6-diyl	-O-	2-furanyl
918	-CH_2-	pyridin-2,6-diyl	-O-	2-thienyl
919	-CH_2-	pyridin-2,6-diyl	CH_2CH_2	2-imidazolyl
920	-CH_2-	pyridin-2,6-diyl	-O-	2-pyridyl

921	$-CH_2-$	pyridin-2,6-diyl	-O-	3-pyridyl
922	$-CH_2-$	pyridin-2,6-diyl	-O-	4-pyridyl
923	$-CH_2-$	pyridin-2,6-diyl	CH_2CH_2	N-morpholinyl
924	$-CH_2-$	pyridin-2,6-diyl	CH_2CH_2	N-piperidinyl
925	$-CH_2-$	pyridin-2,6-diyl	-O-	3-Me-2-pyridyl
926	$-CH_2-$	pyridin-2,6-diyl	-O-	4-Me-2-pyridyl
927	$-CH_2-$	pyridin-2,6-diyl	CH_2CH_2	1-indolyl
928	$-CH_2-$	pyridin-2,6-diyl	-O-	2-benzothienyl
929	$-CH_2-$	pyridin-2,6-diyl	-O-	2-benzofuranyl
930	$-CH_2-$	pyridin-2,6-diyl	CH_2CH_2	1-benzimidazole
931	$-CH_2-$	pyridin-2,6-diyl	-O-	2-naphthyl
932	$-CH_2-$	pyridin-2,4-diyl	-O-	phenyl
933	$-CH_2-$	pyridin-2,4-diyl	-O-	3,3-diphenylmethyl
934	$-CH_2-$	pyridin-2,4-diyl	-O-	2-F-phenyl
935	$-CH_2-$	pyridin-2,4-diyl	-O-	3-F-phenyl
936	$-CH_2-$	pyridin-2,4-diyl	-O-	4-F-phenyl
937	$-CH_2-$	pyridin-2,4-diyl	-O-	2-Cl-phenyl
938	$-CH_2-$	pyridin-2,4-diyl	-O-	3-Cl-phenyl
939	$-CH_2-$	pyridin-2,4-diyl	-O-	4-Cl-phenyl
940	$-CH_2-$	pyridin-2,4-diyl	-O-	2-Me-phenyl
941	$-CH_2-$	pyridin-2,4-diyl	-O-	3-Me-phenyl
942	$-CH_2-$	pyridin-2,4-diyl	-O-	4-Me-phenyl
943	$-CH_2-$	pyridin-2,4-diyl	-O-	2-MeO-phenyl
944	$-CH_2-$	pyridin-2,4-diyl	-O-	3-MeO-phenyl
945	$-CH_2-$	pyridin-2,4-diyl	-O-	4-MeO-phenyl
946	$-CH_2-$	pyridin-2,4-diyl	-O-	2-MeS-phenyl
947	$-CH_2-$	pyridin-2,4-diyl	-O-	3-MeS-phenyl
948	$-CH_2-$	pyridin-2,4-diyl	-O-	4-MeS-phenyl
949	$-CH_2-$	pyridin-2,4-diyl	-O-	2-F_3C-phenyl
950	$-CH_2-$	pyridin-2,4-diyl	-O-	3-F_3C-phenyl
951	$-CH_2-$	pyridin-2,4-diyl	-O-	4-F_3C-phenyl
952	$-CH_2-$	pyridin-2,4-diyl	-O-	2,3-diF-phenyl
953	$-CH_2-$	pyridin-2,4-diyl	-O-	2,4-diF-phenyl
954	$-CH_2-$	pyridin-2,4-diyl	-O-	2,5-diF-phenyl

955	-CH_2-	pyridin-2,4-diyl	-O-	2,6-diF-phenyl
956	-CH_2-	pyridin-2,4-diyl	-O-	3,4-diF-phenyl
957	-CH_2-	pyridin-2,4-diyl	-O-	3,5-diF-phenyl
958	-CH_2-	pyridin-2,4-diyl	-O-	2,3-diCl-phenyl
959	-CH_2-	pyridin-2,4-diyl	-O-	2,4-diCl-phenyl
960	-CH_2-	pyridin-2,4-diyl	-O-	2,5-diCl-phenyl
961	-CH_2-	pyridin-2,4-diyl	-O-	2,6-diCl-phenyl
962	-CH_2-	pyridin-2,4-diyl	-O-	3,4-diCl-phenyl
963	-CH_2-	pyridin-2,4-diyl	-O-	3,5-diCl-phenyl
964	-CH_2-	pyridin-2,4-diyl	-O-	2-Cl-3-F-phenyl
965	-CH_2-	pyridin-2,4-diyl	-O-	2-Cl-4-F-phenyl
966	-CH_2-	pyridin-2,4-diyl	-O-	2-Cl-5-F-phenyl
967	-CH_2-	pyridin-2,4-diyl	-O-	3-Cl-4-F-phenyl
968	-CH_2-	pyridin-2,4-diyl	-O-	3-Cl-5-F-phenyl
969	-CH_2-	pyridin-2,4-diyl	-O-	4-Cl-2-F-phenyl
970	-CH_2-	pyridin-2,4-diyl	-O-	4-Cl-3-F-phenyl
971	-CH_2-	pyridin-2,4-diyl	-O-	2,3-diMeO-phenyl
972	-CH_2-	pyridin-2,4-diyl	-O-	2,4-diMeO-phenyl
973	-CH_2-	pyridin-2,4-diyl	-O-	2,5-diMeO-phenyl
974	-CH_2-	pyridin-2,4-diyl	-O-	2,6-diMeO-phenyl
975	-CH_2-	pyridin-2,4-diyl	-O-	3,4-diMeO-phenyl
976	-CH_2-	pyridin-2,4-diyl	-O-	3,5-diMeO-phenyl
977	-CH_2-	pyridin-2,4-diyl	-O-	cyclopropyl
978	-CH_2-	pyridin-2,4-diyl	-O-	cyclobutyl
979	-CH_2-	pyridin-2,4-diyl	-O-	cyclopentyl
980	-CH_2-	pyridin-2,4-diyl	-O-	cyclohexyl
981	-CH_2-	pyridin-2,4-diyl	-O-	2-furanyl
982	-CH_2-	pyridin-2,4-diyl	-O-	2-thienyl
983	-CH_2-	pyridin-2,4-diyl	CH_2CH_2	2-imidazolyl
984	-CH_2-	pyridin-2,4-diyl	-O-	2-pyridyl
985	-CH_2-	pyridin-2,4-diyl	-O-	3-pyridyl
986	-CH_2-	pyridin-2,4-diyl	-O-	4-pyridyl
987	-CH_2-	pyridin-2,4-diyl	CH_2CH_2	N-morpholinyl
988	-CH_2-	pyridin-2,4-diyl	CH_2CH_2	N-piperidinyl

989	-CH_2-	pyridin-2,4-diyl	-O-	3-Me-2-pyridyl
990	-CH_2-	pyridin-2,4-diyl	-O-	4-Me-2-pyridyl
991	-CH_2-	pyridin-2,4-diyl	CH_2CH_2	1-indolyl
992	-CH_2-	pyridin-2,4-diyl	-O-	2-benzothienyl
993	-CH_2-	pyridin-2,4-diyl	-O-	2-benzofuranyl
994	-CH_2-	pyridin-2,4-diyl	CH_2CH_2	1-benzimidazole
995	-CH_2-	pyridin-2,4-diyl	-O-	2-naphthyl
996	-CH_2-	pyridin-4,2-diyl	-O-	phenyl
997	-CH_2-	pyridin-4,2-diyl	-O-	3,3-diphenylmethyl
998	-CH_2-	pyridin-4,2-diyl	-O-	2-F-phenyl
999	-CH_2-	pyridin-4,2-diyl	-O-	3-F-phenyl
1000	-CH_2-	pyridin-4,2-diyl	-O-	4-F-phenyl
1001	-CH_2-	pyridin-4,2-diyl	-O-	2-Cl-phenyl
1002	-CH_2-	pyridin-4,2-diyl	-O-	3-Cl-phenyl
1003	-CH_2-	pyridin-4,2-diyl	-O-	4-Cl-phenyl
1004	-CH_2-	pyridin-4,2-diyl	-O-	2-Me-phenyl
1005	-CH_2-	pyridin-4,2-diyl	-O-	3-Me-phenyl
1006	-CH_2-	pyridin-4,2-diyl	-O-	4-Me-phenyl
1007	-CH_2-	pyridin-4,2-diyl	-O-	2-MeO-phenyl
1008	-CH_2-	pyridin-4,2-diyl	-O-	3-MeO-phenyl
1009	-CH_2-	pyridin-4,2-diyl	-O-	4-MeO-phenyl
1010	-CH_2-	pyridin-4,2-diyl	-O-	2-MeS-phenyl
1011	-CH_2-	pyridin-4,2-diyl	-O-	3-MeS-phenyl
1012	-CH_2-	pyridin-4,2-diyl	-O-	4-MeS-phenyl
1013	-CH_2-	pyridin-4,2-diyl	-O-	2-F_3C-phenyl
1014	-CH_2-	pyridin-4,2-diyl	-O-	3-F_3C-phenyl
1015	-CH_2-	pyridin-4,2-diyl	-O-	4-F_3C-phenyl
1016	-CH_2-	pyridin-4,2-diyl	-O-	2,3-diF-phenyl
1017	-CH_2-	pyridin-4,2-diyl	-O-	2,4-diF-phenyl
1018	-CH_2-	pyridin-4,2-diyl	-O-	2,5-diF-phenyl
1019	-CH_2-	pyridin-4,2-diyl	-O-	2,6-diF-phenyl
1020	-CH_2-	pyridin-4,2-diyl	-O-	3,4-diF-phenyl
1021	-CH_2-	pyridin-4,2-diyl	-O-	3,5-diF-phenyl
1022	-CH_2-	pyridin-4,2-diyl	-O-	2,3-diCl-phenyl

1023	-CH_2-	pyridin-4,2-diyl	-O-	2,4-diCl-phenyl
1024	-CH_2-	pyridin-4,2-diyl	-O-	2,5-diCl-phenyl
1025	-CH_2-	pyridin-4,2-diyl	-O-	2,6-diCl-phenyl
1026	-CH_2-	pyridin-4,2-diyl	-O-	3,4-diCl-phenyl
1027	-CH_2-	pyridin-4,2-diyl	-O-	3,5-diCl-phenyl
1028	-CH_2-	pyridin-4,2-diyl	-O-	2-Cl-3-F-phenyl
1029	-CH_2-	pyridin-4,2-diyl	-O-	2-Cl-4-F-phenyl
1030	-CH_2-	pyridin-4,2-diyl	-O-	2-Cl-5-F-phenyl
1031	-CH_2-	pyridin-4,2-diyl	-O-	3-Cl-4-F-phenyl
1032	-CH_2-	pyridin-4,2-diyl	-O-	3-Cl-5-F-phenyl
1033	-CH_2-	pyridin-4,2-diyl	-O-	4-Cl-2-F-phenyl
1034	-CH_2-	pyridin-4,2-diyl	-O-	4-Cl-3-F-phenyl
1035	-CH_2-	pyridin-4,2-diyl	-O-	2,3-diMeO-phenyl
1036	-CH_2-	pyridin-4,2-diyl	-O-	2,4-diMeO-phenyl
1037	-CH_2-	pyridin-4,2-diyl	-O-	2,5-diMeO-phenyl
1038	-CH_2-	pyridin-4,2-diyl	-O-	2,6-diMeO-phenyl
1039	-CH_2-	pyridin-4,2-diyl	-O-	3,4-diMeO-phenyl
1040	-CH_2-	pyridin-4,2-diyl	-O-	3,5-diMeO-phenyl
1041	-CH_2-	pyridin-4,2-diyl	-O-	cyclopropyl
1042	-CH_2-	pyridin-4,2-diyl	-O-	cyclobutyl
1043	-CH_2-	pyridin-4,2-diyl	-O-	cyclopentyl
1044	-CH_2-	pyridin-4,2-diyl	-O-	cyclohexyl
1045	-CH_2-	pyridin-4,2-diyl	-O-	2-furanyl
1046	-CH_2-	pyridin-4,2-diyl	-O-	2-thienyl
1047	-CH_2-	pyridin-4,2-diyl	CH_2CH_2	2-imidazolyl
1048	-CH_2-	pyridin-4,2-diyl	-O-	2-pyridyl
1049	-CH_2-	pyridin-4,2-diyl	-O-	3-pyridyl
1050	-CH_2-	pyridin-4,2-diyl	-O-	4-pyridyl
1051	-CH_2-	pyridin-4,2-diyl	CH_2CH_2	N-morpholinyl
1052	-CH_2-	pyridin-4,2-diyl	CH_2CH_2	N-piperidinyl
1053	-CH_2-	pyridin-4,2-diyl	-O-	3-Me-2-pyridyl
1054	-CH_2-	pyridin-4,2-diyl	-O-	4-Me-2-pyridyl
1055	-CH_2-	pyridin-4,2-diyl	CH_2CH_2	1-indolyl
1056	-CH_2-	pyridin-4,2-diyl	-O-	2-benzothienyl

1057	-CH_2-	pyridin-4,2-diyl	-O-	2-benzofuranyl
1058	-CH_2-	pyridin-4,2-diyl	CH_2CH_2	1-benzimidazole
1059	-CH_2-	pyridin-4,2-diyl	-O-	2-naphthyl
1060	-CH_2-	piperidin-1,3-diyl	-O-	phenyl
1061	-CH_2-	piperidin-1,3-diyl	-O-	3,3-diphenylmethyl
1062	-CH_2-	piperidin-1,3-diyl	-O-	2-F-phenyl
1063	-CH_2-	piperidin-1,3-diyl	-O-	3-F-phenyl
1064	-CH_2-	piperidin-1,3-diyl	-O-	4-F-phenyl
1065	-CH_2-	piperidin-1,3-diyl	-O-	2-Cl-phenyl
1066	-CH_2-	piperidin-1,3-diyl	-O-	3-Cl-phenyl
1067	-CH_2-	piperidin-1,3-diyl	-O-	4-Cl-phenyl
1068	-CH_2-	piperidin-1,3-diyl	-O-	2-Me-phenyl
1069	-CH_2-	piperidin-1,3-diyl	-O-	3-Me-phenyl
1070	-CH_2-	piperidin-1,3-diyl	-O-	4-Me-phenyl
1071	-CH_2-	piperidin-1,3-diyl	-O-	2-MeO-phenyl
1072	-CH_2-	piperidin-1,3-diyl	-O-	3-MeO-phenyl
1073	-CH_2-	piperidin-1,3-diyl	-O-	4-MeO-phenyl
1074	-CH_2-	piperidin-1,3-diyl	-O-	2-MeS-phenyl
1075	-CH_2-	piperidin-1,3-diyl	-O-	3-MeS-phenyl
1076	-CH_2-	piperidin-1,3-diyl	-O-	4-MeS-phenyl
1077	-CH_2-	piperidin-1,3-diyl	-O-	2-F_3C-phenyl
1078	-CH_2-	piperidin-1,3-diyl	-O-	3-F_3C-phenyl
1079	-CH_2-	piperidin-1,3-diyl	-O-	4-F_3C-phenyl
1080	-CH_2-	piperidin-1,3-diyl	-O-	2,3-diF-phenyl
1081	-CH_2-	piperidin-1,3-diyl	-O-	2,4-diF-phenyl
1082	-CH_2-	piperidin-1,3-diyl	-O-	2,5-diF-phenyl
1083	-CH_2-	piperidin-1,3-diyl	-O-	2,6-diF-phenyl
1084	-CH_2-	piperidin-1,3-diyl	-O-	3,4-diF-phenyl
1085	-CH_2-	piperidin-1,3-diyl	-O-	3,5-diF-phenyl
1086	-CH_2-	piperidin-1,3-diyl	-O-	2,3-diCl-phenyl
1087	-CH_2-	piperidin-1,3-diyl	-O-	2,4-diCl-phenyl
1088	-CH_2-	piperidin-1,3-diyl	-O-	2,5-diCl-phenyl
1089	-CH_2-	piperidin-1,3-diyl	-O-	2,6-diCl-phenyl
1090	-CH_2-	piperidin-1,3-diyl	-O-	3,4-diCl-phenyl

1091	-CH_2-	piperidin-1,3-diyl	-O-	3,5-diCl-phenyl
1092	-CH_2-	piperidin-1,3-diyl	-O-	2-Cl-3-F-phenyl
1093	-CH_2-	piperidin-1,3-diyl	-O-	2-Cl-4-F-phenyl
1094	-CH_2-	piperidin-1,3-diyl	-O-	2-Cl-5-F-phenyl
1095	-CH_2-	piperidin-1,3-diyl	-O-	3-Cl-4-F-phenyl
1096	-CH_2-	piperidin-1,3-diyl	-O-	3-Cl-5-F-phenyl
1097	-CH_2-	piperidin-1,3-diyl	-O-	4-Cl-2-F-phenyl
1098	-CH_2-	piperidin-1,3-diyl	-O-	4-Cl-3-F-phenyl
1099	-CH_2-	piperidin-1,3-diyl	-O-	2,3-diMeO-phenyl
1100	-CH_2-	piperidin-1,3-diyl	-O-	2,4-diMeO-phenyl
1101	-CH_2-	piperidin-1,3-diyl	-O-	2,5-diMeO-phenyl
1102	-CH_2-	piperidin-1,3-diyl	-O-	2,6-diMeO-phenyl
1103	-CH_2-	piperidin-1,3-diyl	-O-	3,4-diMeO-phenyl
1104	-CH_2-	piperidin-1,3-diyl	-O-	3,5-diMeO-phenyl
1105	-CH_2-	piperidin-1,3-diyl	-O-	Cyclopropyl
1106	-CH_2-	piperidin-1,3-diyl	-O-	Cyclobutyl
1107	-CH_2-	piperidin-1,3-diyl	-O-	Cyclopentyl
1108	-CH_2-	piperidin-1,3-diyl	-O-	Cyclohexyl
1109	-CH_2-	piperidin-1,3-diyl	-O-	2-furanyl
1110	-CH_2-	piperidin-1,3-diyl	-O-	2-thienyl
1111	-CH_2-	piperidin-1,3-diyl	CH_2CH_2	2-imidazolyl
1112	-CH_2-	piperidin-1,3-diyl	-O-	2-pyridyl
1113	-CH_2-	piperidin-1,3-diyl	-O-	3-pyridyl
1114	-CH_2-	piperidin-1,3-diyl	-O-	4-pyridyl
1115	-CH_2-	piperidin-1,3-diyl	CH_2CH_2	N-morpholinyl
1116	-CH_2-	piperidin-1,3-diyl	CH_2CH_2	N-piperidinyl
1117	-CH_2-	piperidin-1,3-diyl	-O-	3-Me-2-pyridyl
1118	-CH_2-	piperidin-1,3-diyl	-O-	4-Me-2-pyridyl
1119	-CH_2-	piperidin-1,3-diyl	CH_2CH_2	1-indolyl
1120	-CH_2-	piperidin-1,3-diyl	-O-	2-benzothienyl
1121	-CH_2-	piperidin-1,3-diyl	-O-	2-benzofuranyl
1122	-CH_2-	piperidin-1,3-diyl	CH_2CH_2	1-benzimidazole
1123	-CH_2-	piperidin-1,3-diyl	-O-	2-naphthyl
1124	-CH_2-	piperidin-3,1-diyl	-O-	Phenyl

1125	-CH_2-	piperidin-3,1-diyl	-O-	3,3-diphenylmethyl
1126	-CH_2-	piperidin-3,1-diyl	-O-	2-F-phenyl
1127	-CH_2-	piperidin-3,1-diyl	-O-	3-F-phenyl
1128	-CH_2-	piperidin-3,1-diyl	-O-	4-F-phenyl
1129	-CH_2-	piperidin-3,1-diyl	-O-	2-Cl-phenyl
1130	-CH_2-	piperidin-3,1-diyl	-O-	3-Cl-phenyl
1131	-CH_2-	piperidin-3,1-diyl	-O-	4-Cl-phenyl
1132	-CH_2-	piperidin-3,1-diyl	-O-	2-Me-phenyl
1133	-CH_2-	piperidin-3,1-diyl	-O-	3-Me-phenyl
1134	-CH_2-	piperidin-3,1-diyl	-O-	4-Me-phenyl
1135	-CH_2-	piperidin-3,1-diyl	-O-	2-MeO-phenyl
1136	-CH_2-	piperidin-3,1-diyl	-O-	3-MeO-phenyl
1137	-CH_2-	piperidin-3,1-diyl	-O-	4-MeO-phenyl
1138	-CH_2-	piperidin-3,1-diyl	-O-	2-MeS-phenyl
1139	-CH_2-	piperidin-3,1-diyl	-O-	3-MeS-phenyl
1140	-CH_2-	piperidin-3,1-diyl	-O-	4-MeS-phenyl
1141	-CH_2-	piperidin-3,1-diyl	-O-	2-F_3C-phenyl
1142	-CH_2-	piperidin-3,1-diyl	-O-	3-F_3C-phenyl
1143	-CH_2-	piperidin-3,1-diyl	-O-	4-F_3C-phenyl
1144	-CH_2-	piperidin-3,1-diyl	-O-	2,3-diF-phenyl
1145	-CH_2-	piperidin-3,1-diyl	-O-	2,4-diF-phenyl
1146	-CH_2-	piperidin-3,1-diyl	-O-	2,5-diF-phenyl
1147	-CH_2-	piperidin-3,1-diyl	-O-	2,6-diF-phenyl
1148	-CH_2-	piperidin-3,1-diyl	-O-	3,4-diF-phenyl
1149	-CH_2-	piperidin-3,1-diyl	-O-	3,5-diF-phenyl
1150	-CH_2-	piperidin-3,1-diyl	-O-	2,3-diCl-phenyl
1151	-CH_2-	piperidin-3,1-diyl	-O-	2,4-diCl-phenyl
1152	-CH_2-	piperidin-3,1-diyl	-O-	2,5-diCl-phenyl
1153	-CH_2-	piperidin-3,1-diyl	-O-	2,6-diCl-phenyl
1154	-CH_2-	piperidin-3,1-diyl	-O-	3,4-diCl-phenyl
1155	-CH_2-	piperidin-3,1-diyl	-O-	3,5-diCl-phenyl
1156	-CH_2-	piperidin-3,1-diyl	-O-	2-Cl-3-F-phenyl
1157	-CH_2-	piperidin-3,1-diyl	-O-	2-Cl-4-F-phenyl
1158	-CH_2-	piperidin-3,1-diyl	-O-	2-Cl-5-F-phenyl

1159	-CH_2-	piperidin-3,1-diyl	-O-	3-Cl-4-F-phenyl
1160	-CH_2-	piperidin-3,1-diyl	-O-	3-Cl-5-F-phenyl
1161	-CH_2-	piperidin-3,1-diyl	-O-	4-Cl-2-F-phenyl
1162	-CH_2-	piperidin-3,1-diyl	-O-	4-Cl-3-F-phenyl
1163	-CH_2-	piperidin-3,1-diyl	-O-	2,3-diMeO-phenyl
1164	-CH_2-	piperidin-3,1-diyl	-O-	2,4-diMeO-phenyl
1165	-CH_2-	piperidin-3,1-diyl	-O-	2,5-diMeO-phenyl
1166	-CH_2-	piperidin-3,1-diyl	-O-	2,6-diMeO-phenyl
1167	-CH_2-	piperidin-3,1-diyl	-O-	3,4-diMeO-phenyl
1168	-CH_2-	piperidin-3,1-diyl	-O-	3,5-diMeO-phenyl
1169	-CH_2-	piperidin-3,1-diyl	-O-	Cyclopropyl
1170	-CH_2-	piperidin-3,1-diyl	-O-	Cyclobutyl
1171	-CH_2-	piperidin-3,1-diyl	-O-	Cyclopentyl
1172	-CH_2-	piperidin-3,1-diyl	-O-	Cyclohexyl
1173	-CH_2-	piperidin-3,1-diyl	-O-	2-furanyl
1174	-CH_2-	piperidin-3,1-diyl	-O-	2-thienyl
1175	-CH_2-	piperidin-3,1-diyl	CH_2CH_2	2-imidazolyl
1176	-CH_2-	piperidin-3,1-diyl	-O-	2-pyridyl
1177	-CH_2-	piperidin-3,1-diyl	-O-	3-pyridyl
1178	-CH_2-	piperidin-3,1-diyl	-O-	4-pyridyl
1179	-CH_2-	piperidin-3,1-diyl	CH_2CH_2	N-morpholinyl
1180	-CH_2-	piperidin-3,1-diyl	CH_2CH_2	N-piperidinyl
1181	-CH_2-	piperidin-3,1-diyl	-O-	3-Me-2-pyridyl
1182	-CH_2-	piperidin-3,1-diyl	-O-	4-Me-2-pyridyl
1183	-CH_2-	piperidin-3,1-diyl	CH_2CH_2	1-indolyl
1184	-CH_2-	piperidin-3,1-diyl	-O-	2-benzothienyl
1185	-CH_2-	piperidin-3,1-diyl	-O-	2-benzofuranyl
1186	-CH_2-	piperidin-3,1-diyl	CH_2CH_2	1-benzimidazole
1187	-CH_2-	piperidin-3,1-diyl	-O-	2-naphthyl
1188	-CH_2-	cyclohex-1,3-diyl	-O-	Phenyl
1189	-CH_2-	cyclohex-1,3-diyl	-O-	3,3-diphenylmethyl
1190	-CH_2-	cyclohex-1,3-diyl	-O-	2-F-phenyl
1191	-CH_2-	cyclohex-1,3-diyl	-O-	3-F-phenyl
1192	-CH_2-	cyclohex-1,3-diyl	-O-	4-F-phenyl

1193	-CH_2-	cyclohex-1,3-diyl	-O-	2-Cl-phenyl
1194	-CH_2-	cyclohex-1,3-diyl	-O-	3-Cl-phenyl
1195	-CH_2-	cyclohex-1,3-diyl	-O-	4-Cl-phenyl
1196	-CH_2-	cyclohex-1,3-diyl	-O-	2-Me-phenyl
1197	-CH_2-	cyclohex-1,3-diyl	-O-	3-Me-phenyl
1198	-CH_2-	cyclohex-1,3-diyl	-O-	4-Me-phenyl
1199	-CH_2-	cyclohex-1,3-diyl	-O-	2-MeO-phenyl
1200	-CH_2-	cyclohex-1,3-diyl	-O-	3-MeO-phenyl
1201	-CH_2-	cyclohex-1,3-diyl	-O-	4-MeO-phenyl
1202	-CH_2-	cyclohex-1,3-diyl	-O-	2-MeS-phenyl
1203	-CH_2-	cyclohex-1,3-diyl	-O-	3-MeS-phenyl
1204	-CH_2-	cyclohex-1,3-diyl	-O-	4-MeS-phenyl
1205	-CH_2-	cyclohex-1,3-diyl	-O-	2-F_3C-phenyl
1206	-CH_2-	cyclohex-1,3-diyl	-O-	3-F_3C-phenyl
1207	-CH_2-	cyclohex-1,3-diyl	-O-	4-F_3C-phenyl
1208	-CH_2-	cyclohex-1,3-diyl	-O-	2,3-diF-phenyl
1209	-CH_2-	cyclohex-1,3-diyl	-O-	2,4-diF-phenyl
1210	-CH_2-	cyclohex-1,3-diyl	-O-	2,5-diF-phenyl
1211	-CH_2-	cyclohex-1,3-diyl	-O-	2,6-diF-phenyl
1212	-CH_2-	cyclohex-1,3-diyl	-O-	3,4-diF-phenyl
1213	-CH_2-	cyclohex-1,3-diyl	-O-	3,5-diF-phenyl
1214	-CH_2-	cyclohex-1,3-diyl	-O-	2,3-diCl-phenyl
1215	-CH_2-	cyclohex-1,3-diyl	-O-	2,4-diCl-phenyl
1216	-CH_2-	cyclohex-1,3-diyl	-O-	2,5-diCl-phenyl
1217	-CH_2-	cyclohex-1,3-diyl	-O-	2,6-diCl-phenyl
1218	-CH_2-	cyclohex-1,3-diyl	-O-	3,4-diCl-phenyl
1219	-CH_2-	cyclohex-1,3-diyl	-O-	3,5-diCl-phenyl
1220	-CH_2-	cyclohex-1,3-diyl	-O-	2-Cl-3-F-phenyl
1221	-CH_2-	cyclohex-1,3-diyl	-O-	2-Cl-4-F-phenyl
1222	-CH_2-	cyclohex-1,3-diyl	-O-	2-Cl-5-F-phenyl
1223	-CH_2-	cyclohex-1,3-diyl	-O-	3-Cl-4-F-phenyl
1224	-CH_2-	cyclohex-1,3-diyl	-O-	3-Cl-5-F-phenyl
1225	-CH_2-	cyclohex-1,3-diyl	-O-	4-Cl-2-F-phenyl
1226	-CH_2-	cyclohex-1,3-diyl	-O-	4-Cl-3-F-phenyl

1227	$-CH_2-$	cyclohex-1,3-diyl	-O-	2,3-diMeO-phenyl
1228	$-CH_2-$	cyclohex-1,3-diyl	-O-	2,4-diMeO-phenyl
1229	$-CH_2-$	cyclohex-1,3-diyl	-O-	2,5-diMeO-phenyl
1230	$-CH_2-$	cyclohex-1,3-diyl	-O-	2,6-diMeO-phenyl
1231	$-CH_2-$	cyclohex-1,3-diyl	-O-	3,4-diMeO-phenyl
1232	$-CH_2-$	cyclohex-1,3-diyl	-O-	3,5-diMeO-phenyl
1233	$-CH_2-$	cyclohex-1,3-diyl	-O-	Cyclopropyl
1234	$-CH_2-$	cyclohex-1,3-diyl	-O-	Cyclobutyl
1235	$-CH_2-$	cyclohex-1,3-diyl	-O-	Cyclopentyl
1236	$-CH_2-$	cyclohex-1,3-diyl	-O-	Cyclohexyl
1237	$-CH_2-$	cyclohex-1,3-diyl	-O-	2-furanyl
1238	$-CH_2-$	cyclohex-1,3-diyl	-O-	2-thienyl
1239	$-CH_2-$	cyclohex-1,3-diyl	CH_2CH_2	2-imidazolyl
1240	$-CH_2-$	cyclohex-1,3-diyl	-O-	2-pyridyl
1241	$-CH_2-$	cyclohex-1,3-diyl	-O-	3-pyridyl
1242	$-CH_2-$	cyclohex-1,3-diyl	-O-	4-pyridyl
1243	$-CH_2-$	cyclohex-1,3-diyl	CH_2CH_2	N-morpholinyl
1244	$-CH_2-$	cyclohex-1,3-diyl	CH_2CH_2	N-piperidinyl
1245	$-CH_2-$	cyclohex-1,3-diyl	-O-	3-Me-2-pyridyl
1246	$-CH_2-$	cyclohex-1,3-diyl	-O-	4-Me-2-pyridyl
1247	$-CH_2-$	cyclohex-1,3-diyl	CH_2CH_2	1-indolyl
1248	$-CH_2-$	cyclohex-1,3-diyl	-O-	2-benzothienyl
1249	$-CH_2-$	cyclohex-1,3-diyl	-O-	2-benzofuranyl
1250	$-CH_2-$	cyclohex-1,3-diyl	CH_2CH_2	1-benzimidazole
1251	$-CH_2-$	cyclohex-1,3-diyl	-O-	2-naphthyl
1252	$-CH_2-$	cyclopropan-1,2-diyl	-O-	Phenyl
1253	$-CH_2-$	cyclopropan-1,2-diyl	-O-	3,3-diphenylmethyl
1254	$-CH_2-$	cyclopropan-1,2-diyl	-O-	2-F-phenyl
1255	$-CH_2-$	cyclopropan-1,2-diyl	-O-	3-F-phenyl
1256	$-CH_2-$	cyclopropan-1,2-diyl	-O-	4-F-phenyl
1257	$-CH_2-$	cyclopropan-1,2-diyl	-O-	2-Cl-phenyl
1258	$-CH_2-$	cyclopropan-1,2-diyl	-O-	3-Cl-phenyl
1259	$-CH_2-$	cyclopropan-1,2-diyl	-O-	4-Cl-phenyl
1260	$-CH_2-$	cyclopropan-1,2-diyl	-O-	2-Me-phenyl

1261	-CH_2-	cyclopropan-1,2-diyl	-O-	3-Me-phenyl
1262	-CH_2-	cyclopropan-1,2-diyl	-O-	4-Me-phenyl
1263	-CH_2-	cyclopropan-1,2-diyl	-O-	2-MeO-phenyl
1264	-CH_2-	cyclopropan-1,2-diyl	-O-	3-MeO-phenyl
1265	-CH_2-	cyclopropan-1,2-diyl	-O-	4-MeO-phenyl
1266	-CH_2-	cyclopropan-1,2-diyl	-O-	2-MeS-phenyl
1267	-CH_2-	cyclopropan-1,2-diyl	-O-	3-MeS-phenyl
1268	-CH_2-	cyclopropan-1,2-diyl	-O-	4-MeS-phenyl
1269	-CH_2-	cyclopropan-1,2-diyl	-O-	2-F_3C-phenyl
1270	-CH_2-	cyclopropan-1,2-diyl	-O-	3-F_3C-phenyl
1271	-CH_2-	cyclopropan-1,2-diyl	-O-	4-F_3C-phenyl
1272	-CH_2-	cyclopropan-1,2-diyl	-O-	2,3-diF-phenyl
1273	-CH_2-	cyclopropan-1,2-diyl	-O-	2,4-diF-phenyl
1274	-CH_2-	cyclopropan-1,2-diyl	-O-	2,5-diF-phenyl
1275	-CH_2-	cyclopropan-1,2-diyl	-O-	2,6-diF-phenyl
1276	-CH_2-	cyclopropan-1,2-diyl	-O-	3,4-diF-phenyl
1277	-CH_2-	cyclopropan-1,2-diyl	-O-	3,5-diF-phenyl
1278	-CH_2-	cyclopropan-1,2-diyl	-O-	2,3-diCl-phenyl
1279	-CH_2-	cyclopropan-1,2-diyl	-O-	2,4-diCl-phenyl
1280	-CH_2-	cyclopropan-1,2-diyl	-O-	2,5-diCl-phenyl
1281	-CH_2-	cyclopropan-1,2-diyl	-O-	2,6-diCl-phenyl
1282	-CH_2-	cyclopropan-1,2-diyl	-O-	3,4-diCl-phenyl
1283	-CH_2-	cyclopropan-1,2-diyl	-O-	3,5-diCl-phenyl
1284	-CH_2-	cyclopropan-1,2-diyl	-O-	2-Cl-3-F-phenyl
1285	-CH_2-	cyclopropan-1,2-diyl	-O-	2-Cl-4-F-phenyl
1286	-CH_2-	cyclopropan-1,2-diyl	-O-	2-Cl-5-F-phenyl
1287	-CH_2-	cyclopropan-1,2-diyl	-O-	3-Cl-4-F-phenyl
1288	-CH_2-	cyclopropan-1,2-diyl	-O-	3-Cl-5-F-phenyl
1289	-CH_2-	cyclopropan-1,2-diyl	-O-	4-Cl-2-F-phenyl
1290	-CH_2-	cyclopropan-1,2-diyl	-O-	4-Cl-3-F-phenyl
1291	-CH_2-	cyclopropan-1,2-diyl	-O-	2,3-diMeO-phenyl
1292	-CH_2-	cyclopropan-1,2-diyl	-O-	2,4-diMeO-phenyl
1293	-CH_2-	cyclopropan-1,2-diyl	-O-	2,5-diMeO-phenyl
1294	-CH_2-	cyclopropan-1,2-diyl	-O-	2,6-diMeO-phenyl

1295	-CH_2-	cyclopropan-1,2-diyl	-O-	3,4-diMeO-phenyl
1296	-CH_2-	cyclopropan-1,2-diyl	-O-	3,5-diMeO-phenyl
1297	-CH_2-	cyclopropan-1,2-diyl	-O-	Cyclopropyl
1298	-CH_2-	cyclopropan-1,2-diyl	-O-	Cyclobutyl
1299	-CH_2-	cyclopropan-1,2-diyl	-O-	Cyclopentyl
1300	-CH_2-	cyclopropan-1,2-diyl	-O-	Cyclohexyl
1301	-CH_2-	cyclopropan-1,2-diyl	-O-	2-furanyl
1302	-CH_2-	cyclopropan-1,2-diyl	-O-	2-thienyl
1303	-CH_2-	cyclopropan-1,2-diyl	CH_2CH_2	2-imidazolyl
1304	-CH_2-	cyclopropan-1,2-diyl	-O-	2-pyridyl
1305	-CH_2-	cyclopropan-1,2-diyl	-O-	3-pyridyl
1306	-CH_2-	cyclopropan-1,2-diyl	-O-	4-pyridyl
1307	-CH_2-	cyclopropan-1,2-diyl	CH_2CH_2	N-morpholinyl
1308	-CH_2-	cyclopropan-1,2-diyl	CH_2CH_2	N-piperidinyl
1309	-CH_2-	cyclopropan-1,2-diyl	-O-	3-Me-2-pyridyl
1310	-CH_2-	cyclopropan-1,2-diyl	-O-	4-Me-2-pyridyl
1311	-CH_2-	cyclopropan-1,2-diyl	CH_2CH_2	1-indolyl
1312	-CH_2-	cyclopropan-1,2-diyl	-O-	2-benzothienyl
1313	-CH_2-	cyclopropan-1,2-diyl	-O-	2-benzofuranyl
1314	-CH_2-	cyclopropan-1,2-diyl	CH_2CH_2	1-benzimidazole
1315	-CH_2-	cyclopropan-1,2-diyl	-O-	2-naphthyl
1316	-CH_2-	cyclopentan-1,3-diyl	-O-	Phenyl
1317	-CH_2-	cyclopentan-1,3-diyl	-O-	3,3-diphenylmethyl
1318	-CH_2-	cyclopentan-1,3-diyl	-O-	2-F-phenyl
1319	-CH_2-	cyclopentan-1,3-diyl	-O-	3-F-phenyl
1320	-CH_2-	cyclopentan-1,3-diyl	-O-	4-F-phenyl
1321	-CH_2-	cyclopentan-1,3-diyl	-O-	2-Cl-phenyl
1322	-CH_2-	cyclopentan-1,3-diyl	-O-	3-Cl-phenyl
1323	-CH_2-	cyclopentan-1,3-diyl	-O-	4-Cl-phenyl
1324	-CH_2-	cyclopentan-1,3-diyl	-O-	2-Me-phenyl
1325	-CH_2-	cyclopentan-1,3-diyl	-O-	3-Me-phenyl
1326	-CH_2-	cyclopentan-1,3-diyl	-O-	4-Me-phenyl
1327	-CH_2-	cyclopentan-1,3-diyl	-O-	2-MeO-phenyl
1328	-CH_2-	cyclopentan-1,3-diyl	-O-	3-MeO-phenyl

1329	-CH_2-	cyclopentan-1,3-diyl	-O-	4-MeO-phenyl
1330	-CH_2-	cyclopentan-1,3-diyl	-O-	2-MeS-phenyl
1331	-CH_2-	cyclopentan-1,3-diyl	-O-	3-MeS-phenyl
1332	-CH_2-	cyclopentan-1,3-diyl	-O-	4-MeS-phenyl
1333	-CH_2-	cyclopentan-1,3-diyl	-O-	2-F_3C-phenyl
1334	-CH_2-	cyclopentan-1,3-diyl	-O-	3-F_3C-phenyl
1335	-CH_2-	cyclopentan-1,3-diyl	-O-	4-F_3C-phenyl
1336	-CH_2-	cyclopentan-1,3-diyl	-O-	2,3-diF-phenyl
1337	-CH_2-	cyclopentan-1,3-diyl	-O-	2,4-diF-phenyl
1338	-CH_2-	cyclopentan-1,3-diyl	-O-	2,5-diF-phenyl
1339	-CH_2-	cyclopentan-1,3-diyl	-O-	2,6-diF-phenyl
1340	-CH_2-	cyclopentan-1,3-diyl	-O-	3,4-diF-phenyl
1341	-CH_2-	cyclopentan-1,3-diyl	-O-	3,5-diF-phenyl
1342	-CH_2-	cyclopentan-1,3-diyl	-O-	2,3-diCl-phenyl
1343	-CH_2-	cyclopentan-1,3-diyl	-O-	2,4-diCl-phenyl
1344	-CH_2-	cyclopentan-1,3-diyl	-O-	2,5-diCl-phenyl
1345	-CH_2-	cyclopentan-1,3-diyl	-O-	2,6-diCl-phenyl
1346	-CH_2-	cyclopentan-1,3-diyl	-O-	3,4-diCl-phenyl
1347	-CH_2-	cyclopentan-1,3-diyl	-O-	3,5-diCl-phenyl
1348	-CH_2-	cyclopentan-1,3-diyl	-O-	2-Cl-3-F-phenyl
1349	-CH_2-	cyclopentan-1,3-diyl	-O-	2-Cl-4-F-phenyl
1350	-CH_2-	cyclopentan-1,3-diyl	-O-	2-Cl-5-F-phenyl
1351	-CH_2-	cyclopentan-1,3-diyl	-O-	3-Cl-4-F-phenyl
1352	-CH_2-	cyclopentan-1,3-diyl	-O-	3-Cl-5-F-phenyl
1353	-CH_2-	cyclopentan-1,3-diyl	-O-	4-Cl-2-F-phenyl
1354	-CH_2-	cyclopentan-1,3-diyl	-O-	4-Cl-3-F-phenyl
1355	-CH_2-	cyclopentan-1,3-diyl	-O-	2,3-diMeO-phenyl
1356	-CH_2-	cyclopentan-1,3-diyl	-O-	2,4-diMeO-phenyl
1357	-CH_2-	cyclopentan-1,3-diyl	-O-	2,5-diMeO-phenyl
1358	-CH_2-	cyclopentan-1,3-diyl	-O-	2,6-diMeO-phenyl
1359	-CH_2-	cyclopentan-1,3-diyl	-O-	3,4-diMeO-phenyl
1360	-CH_2-	cyclopentan-1,3-diyl	-O-	3,5-diMeO-phenyl
1361	-CH_2-	cyclopentan-1,3-diyl	-O-	Cyclopropyl
1362	-CH_2-	cyclopentan-1,3-diyl	-O-	Cyclobutyl

1363	-CH_2-	cyclopentan-1,3-diyl	-O-	Cyclopentyl
1364	-CH_2-	cyclopentan-1,3-diyl	-O-	Cyclohexyl
1365	-CH_2-	cyclopentan-1,3-diyl	-O-	2-furanyl
1366	-CH_2-	cyclopentan-1,3-diyl	-O-	2-thienyl
1367	-CH_2-	cyclopentan-1,3-diyl	CH_2CH_2	2-imidazolyl
1368	-CH_2-	cyclopentan-1,3-diyl	-O-	2-pyridyl
1369	-CH_2-	cyclopentan-1,3-diyl	-O-	3-pyridyl
1370	-CH_2-	cyclopentan-1,3-diyl	-O-	4-pyridyl
1371	-CH_2-	cyclopentan-1,3-diyl	CH_2CH_2	N-morpholinyl
1372	-CH_2-	cyclopentan-1,3-diyl	CH_2CH_2	N-piperidinyl
1373	-CH_2-	cyclopentan-1,3-diyl	-O-	3-Me-2-pyridyl
1374	-CH_2-	cyclopentan-1,3-diyl	-O-	4-Me-2-pyridyl
1375	-CH_2-	cyclopentan-1,3-diyl	CH_2CH_2	1-indolyl
1376	-CH_2-	cyclopentan-1,3-diyl	-O-	2-benzothienyl
1377	-CH_2-	cyclopentan-1,3-diyl	-O-	2-benzofuranyl
1378	-CH_2-	cyclopentan-1,3-diyl	CH_2CH_2	1-benzimidazole
1379	-CH_2-	cyclopentan-1,3-diyl	-O-	2-naphthyl

1380	-CH_2-	bond	bond	phenyl
1381	-CH_2-	bond	bond	3,3-diphenyl
1382	-CH_2-	bond	bond	2-F-phenyl
1383	-CH_2-	bond	bond	3-F-phenyl
1384	-CH_2-	bond	bond	4-F-phenyl
1385	-CH_2-	bond	bond	2-Cl-phenyl
1386	-CH_2-	bond	bond	3-Cl-phenyl
1387	-CH_2-	bond	bond	4-Cl-phenyl
1388	-CH_2-	bond	bond	2-Me-phenyl
1389	-CH_2-	bond	bond	3-Me-phenyl
1390	-CH_2-	bond	bond	4-Me-phenyl
1391	-CH_2-	bond	bond	2-MeO-phenyl
1392	-CH_2-	bond	bond	3-MeO-phenyl
1393	-CH_2-	bond	bond	4-MeO-phenyl
1394	-CH_2-	bond	bond	2-MeS-phenyl

1395	$-CH_2-$	bond	bond	3-MeS-phenyl
1396	$-CH_2-$	bond	bond	4-MeS-phenyl
1397	$-CH_2-$	bond	bond	2-F_3C-phenyl
1398	$-CH_2-$	bond	bond	3-F_3C-phenyl
1399	$-CH_2-$	bond	bond	4-F_3C-phenyl
1400	$-CH_2-$	bond	bond	2,3-diF-phenyl
1401	$-CH_2-$	bond	bond	2,4-diF-phenyl
1402	$-CH_2-$	bond	bond	2,5-diF-phenyl
1403	$-CH_2-$	bond	bond	2,6-diF-phenyl
1404	$-CH_2-$	bond	bond	3,4-diF-phenyl
1405	$-CH_2-$	bond	bond	3,5-diF-phenyl
1406	$-CH_2-$	bond	bond	2,3-diCl-phenyl
1407	$-CH_2-$	bond	bond	2,4-diCl-phenyl
1408	$-CH_2-$	bond	bond	2,5-diCl-phenyl
1409	$-CH_2-$	bond	bond	2,6-diCl-phenyl
1410	$-CH_2-$	bond	bond	3,4-diCl-phenyl
1411	$-CH_2-$	bond	bond	3,5-diCl-phenyl
1412	$-CH_2-$	bond	bond	2-Cl-3-F-phenyl
1413	$-CH_2-$	bond	bond	2-Cl-4-F-phenyl
1414	$-CH_2-$	bond	bond	2-Cl-5-F-phenyl
1415	$-CH_2-$	bond	bond	3-Cl-4-F-phenyl
1416	$-CH_2-$	bond	bond	3-Cl-5-F-phenyl
1417	$-CH_2-$	bond	bond	4-Cl-2-F-phenyl
1418	$-CH_2-$	bond	bond	4-Cl-3-F-phenyl
1419	$-CH_2-$	bond	bond	2,3-diMeO-phenyl
1420	$-CH_2-$	bond	bond	2,4-diMeO-phenyl
1421	$-CH_2-$	bond	bond	2,5-diMeO-phenyl
1422	$-CH_2-$	bond	bond	2,6-diMeO-phenyl
1423	$-CH_2-$	bond	bond	3,4-diMeO-phenyl
1424	$-CH_2-$	bond	bond	3,5-diMeO-phenyl
1425	$-CH_2-$	bond	bond	cyclopropyl
1426	$-CH_2-$	bond	bond	cyclobutyl
1427	$-CH_2-$	bond	bond	cyclopentyl
1428	$-CH_2-$	bond	bond	cyclohexyl

1429	$-CH_2-$	bond	bond	2-furanyl
1430	$-CH_2-$	bond	bond	2-thienyl
1431	$-CH_2-$	bond	bond	2-imidazolyl
1432	$-CH_2-$	bond	bond	2-pyridyl
1433	$-CH_2-$	bond	bond	3-pyridyl
1434	$-CH_2-$	bond	bond	4-pyridyl
1435	$-CH_2-$	bond	bond	N-morpholinyl
1436	$-CH_2-$	bond	bond	N-piperidinyl
1437	$-CH_2-$	bond	bond	3-Me-2-pyridyl
1438	$-CH_2-$	bond	bond	4-Me-2-pyridyl
1439	$-CH_2-$	bond	bond	1-indolyl
1440	$-CH_2-$	bond	bond	2-benzothienyl
1441	$-CH_2-$	bond	bond	2-benzofuranyl
1442	$-CH_2-$	bond	bond	1-benzimidazole
1443	$-CH_2-$	bond	bond	2-naphthyl
1444	$-CH_2CH_2-$	bond	bond	phenyl
1445	$-CH_2CH_2-$	bond	bond	3,3-diphenyl
1446	$-CH_2CH_2-$	bond	bond	2-F-phenyl
1447	$-CH_2CH_2-$	bond	bond	3-F-phenyl
1448	$-CH_2CH_2-$	bond	bond	4-F-phenyl
1449	$-CH_2CH_2-$	bond	bond	2-Cl-phenyl
1450	$-CH_2CH_2-$	bond	bond	3-Cl-phenyl
1451	$-CH_2CH_2-$	bond	bond	4-Cl-phenyl
1452	$-CH_2CH_2-$	bond	bond	2-Me-phenyl
1453	$-CH_2CH_2-$	bond	bond	3-Me-phenyl
1454	$-CH_2CH_2-$	bond	bond	4-Me-phenyl
1455	$-CH_2CH_2-$	bond	bond	2-MeO-phenyl
1456	$-CH_2CH_2-$	bond	bond	3-MeO-phenyl
1457	$-CH_2CH_2-$	bond	bond	4-MeO-phenyl
1458	$-CH_2CH_2-$	bond	bond	2-MeS-phenyl
1459	$-CH_2CH_2-$	bond	bond	3-MeS-phenyl
1460	$-CH_2CH_2-$	bond	bond	4-MeS-phenyl
1461	$-CH_2CH_2-$	bond	bond	2-F_3C-phenyl
1462	$-CH_2CH_2-$	bond	bond	3-F_3C-phenyl

1463	$-CH_2CH_2-$	bond	bond	4-F_3C-phenyl
1464	$-CH_2CH_2-$	bond	bond	2,3-diF-phenyl
1465	$-CH_2CH_2-$	bond	bond	2,4-diF-phenyl
1466	$-CH_2CH_2-$	bond	bond	2,5-diF-phenyl
1467	$-CH_2CH_2-$	bond	bond	2,6-diF-phenyl
1468	$-CH_2CH_2-$	bond	bond	3,4-diF-phenyl
1469	$-CH_2CH_2-$	bond	bond	3,5-diF-phenyl
1470	$-CH_2CH_2-$	bond	bond	2,3-diCl-phenyl
1471	$-CH_2CH_2-$	bond	bond	2,4-diCl-phenyl
1472	$-CH_2CH_2-$	bond	bond	2,5-diCl-phenyl
1473	$-CH_2CH_2-$	bond	bond	2,6-diCl-phenyl
1474	$-CH_2CH_2-$	bond	bond	3,4-diCl-phenyl
1475	$-CH_2CH_2-$	bond	bond	3,5-diCl-phenyl
1476	$-CH_2CH_2-$	bond	bond	2-Cl-3-F-phenyl
1477	$-CH_2CH_2-$	bond	bond	2-Cl-4-F-phenyl
1478	$-CH_2CH_2-$	bond	bond	2-Cl-5-F-phenyl
1479	$-CH_2CH_2-$	bond	bond	3-Cl-4-F-phenyl
1480	$-CH_2CH_2-$	bond	bond	3-Cl-5-F-phenyl
1481	$-CH_2CH_2-$	bond	bond	4-Cl-2-F-phenyl
1482	$-CH_2CH_2-$	bond	bond	4-Cl-3-F-phenyl
1483	$-CH_2CH_2-$	bond	bond	2,3-diMeO-phenyl
1484	$-CH_2CH_2-$	bond	bond	2,4-diMeO-phenyl
1485	$-CH_2CH_2-$	bond	bond	2,5-diMeO-phenyl
1486	$-CH_2CH_2-$	bond	bond	2,6-diMeO-phenyl
1487	$-CH_2CH_2-$	bond	bond	3,4-diMeO-phenyl
1488	$-CH_2CH_2-$	bond	bond	3,5-diMeO-phenyl
1489	$-CH_2CH_2-$	bond	bond	cyclopropyl
1490	$-CH_2CH_2-$	bond	bond	cyclobutyl
1491	$-CH_2CH_2-$	bond	bond	cyclopentyl
1492	$-CH_2CH_2-$	bond	bond	cyclohexyl
1493	$-CH_2CH_2-$	bond	bond	2-furanyl
1494	$-CH_2CH_2-$	bond	bond	2-thienyl
1495	$-CH_2CH_2-$	bond	bond	2-imidazolyl
1496	$-CH_2CH_2-$	bond	bond	2-pyridyl

1497	$-CH_2CH_2-$	bond	bond	3-pyridyl
1498	$-CH_2CH_2-$	bond	bond	4-pyridyl
1499	$-CH_2CH_2-$	bond	bond	N-morpholinyl
1500	$-CH_2CH_2-$	bond	bond	N-piperidinyl
1501	$-CH_2CH_2-$	bond	bond	3-Me-2-pyridyl
1502	$-CH_2CH_2-$	bond	bond	4-Me-2-pyridyl
1503	$-CH_2CH_2-$	bond	bond	1-indolyl
1504	$-CH_2CH_2-$	bond	bond	2-benzothienyl
1505	$-CH_2CH_2-$	bond	bond	2-benzofuranyl
1506	$-CH_2CH_2-$	bond	bond	1-benzimidazole
1507	$-CH_2CH_2-$	bond	bond	2-naphthyl
1508	$-CH_2CH_2CH_2-$	bond	bond	phenyl
1509	$-CH_2CH_2CH_2-$	bond	bond	3,3-diphenyl
1510	$-CH_2CH_2CH_2-$	bond	bond	2-F-phenyl
1511	$-CH_2CH_2CH_2-$	bond	bond	3-F-phenyl
1512	$-CH_2CH_2CH_2-$	bond	bond	4-F-phenyl
1513	$-CH_2CH_2CH_2-$	bond	bond	2-Cl-phenyl
1514	$-CH_2CH_2CH_2-$	bond	bond	3-Cl-phenyl
1515	$-CH_2CH_2CH_2-$	bond	bond	4-Cl-phenyl
1516	$-CH_2CH_2CH_2-$	bond	bond	2-Me-phenyl
1517	$-CH_2CH_2CH_2-$	bond	bond	3-Me-phenyl
1518	$-CH_2CH_2CH_2-$	bond	bond	4-Me-phenyl
1519	$-CH_2CH_2CH_2-$	bond	bond	2-MeO-phenyl
1520	$-CH_2CH_2CH_2-$	bond	bond	3-MeO-phenyl
1521	$-CH_2CH_2CH_2-$	bond	bond	4-MeO-phenyl
1522	$-CH_2CH_2CH_2-$	bond	bond	2-MeS-phenyl
1523	$-CH_2CH_2CH_2-$	bond	bond	3-MeS-phenyl
1524	$-CH_2CH_2CH_2-$	bond	bond	4-MeS-phenyl
1525	$-CH_2CH_2CH_2-$	bond	bond	2-F_3C-phenyl
1526	$-CH_2CH_2CH_2-$	bond	bond	3-F_3C-phenyl
1527	$-CH_2CH_2CH_2-$	bond	bond	4-F_3C-phenyl
1528	$-CH_2CH_2CH_2-$	bond	bond	2,3-diF-phenyl
1529	$-CH_2CH_2CH_2-$	bond	bond	2,4-diF-phenyl
1530	$-CH_2CH_2CH_2-$	bond	bond	2,5-diF-phenyl

1531	$-CH_2CH_2CH_2-$	bond	bond	2,6-diF-phenyl
1532	$-CH_2CH_2CH_2-$	bond	bond	3,4-diF-phenyl
1533	$-CH_2CH_2CH_2-$	bond	bond	3,5-diF-phenyl
1534	$-CH_2CH_2CH_2-$	bond	bond	2,3-diCl-phenyl
1535	$-CH_2CH_2CH_2-$	bond	bond	2,4-diCl-phenyl
1536	$-CH_2CH_2CH_2-$	bond	bond	2,5-diCl-phenyl
1537	$-CH_2CH_2CH_2-$	bond	bond	2,6-diCl-phenyl
1538	$-CH_2CH_2CH_2-$	bond	bond	3,4-diCl-phenyl
1539	$-CH_2CH_2CH_2-$	bond	bond	3,5-diCl-phenyl
1540	$-CH_2CH_2CH_2-$	bond	bond	2-Cl-3-F-phenyl
1541	$-CH_2CH_2CH_2-$	bond	bond	2-Cl-4-F-phenyl
1542	$-CH_2CH_2CH_2-$	bond	bond	2-Cl-5-F-phenyl
1543	$-CH_2CH_2CH_2-$	bond	bond	3-Cl-4-F-phenyl
1544	$-CH_2CH_2CH_2-$	bond	bond	3-Cl-5-F-phenyl
1545	$-CH_2CH_2CH_2-$	bond	bond	4-Cl-2-F-phenyl
1546	$-CH_2CH_2CH_2-$	bond	bond	4-Cl-3-F-phenyl
1547	$-CH_2CH_2CH_2-$	bond	bond	2,3-diMeO-phenyl
1548	$-CH_2CH_2CH_2-$	bond	bond	2,4-diMeO-phenyl
1549	$-CH_2CH_2CH_2-$	bond	bond	2,5-diMeO-phenyl
1550	$-CH_2CH_2CH_2-$	bond	bond	2,6-diMeO-phenyl
1551	$-CH_2CH_2CH_2-$	bond	bond	3,4-diMeO-phenyl
1552	$-CH_2CH_2CH_2-$	bond	bond	3,5-diMeO-phenyl
1553	$-CH_2CH_2CH_2-$	bond	bond	cyclopropyl
1554	$-CH_2CH_2CH_2-$	bond	bond	cyclobutyl
1555	$-CH_2CH_2CH_2-$	bond	bond	cyclopentyl
1556	$-CH_2CH_2CH_2-$	bond	bond	cyclohexyl
1557	$-CH_2CH_2CH_2-$	bond	bond	2-furanyl
1558	$-CH_2CH_2CH_2-$	bond	bond	2-thienyl
1559	$-CH_2CH_2CH_2-$	bond	bond	2-imidazolyl
1560	$-CH_2CH_2CH_2-$	bond	bond	2-pyridyl
1561	$-CH_2CH_2CH_2-$	bond	bond	3-pyridyl
1562	$-CH_2CH_2CH_2-$	bond	bond	4-pyridyl
1563	$-CH_2CH_2CH_2-$	bond	bond	N-morpholinyl
1564	$-CH_2CH_2CH_2-$	bond	bond	N-piperidinyl

1565	$-CH_2CH_2CH_2-$	bond	bond	3-Me-2-pyridyl
1566	$-CH_2CH_2CH_2-$	bond	bond	4-Me-2-pyridyl
1567	$-CH_2CH_2CH_2-$	bond	bond	1-indolyl
1568	$-CH_2CH_2CH_2-$	bond	bond	2-benzothienyl
1569	$-CH_2CH_2CH_2-$	bond	bond	2-benzofuranyl
1570	$-CH_2CH_2CH_2-$	bond	bond	1-benzimidazole
1571	$-CH_2CH_2CH_2-$	bond	bond	2-naphthyl
1572	$-CH_2CH_2-$	bond	-O-	phenyl
1573	$-CH_2CH_2-$	bond	-O-	3,3-diphenylmethyl
1574	$-CH_2CH_2-$	bond	-O-	2-F-phenyl
1575	$-CH_2CH_2-$	bond	-O-	3-F-phenyl
1576	$-CH_2CH_2-$	bond	-O-	4-F-phenyl
1577	$-CH_2CH_2-$	bond	-O-	2-Cl-phenyl
1578	$-CH_2CH_2-$	bond	-O-	3-Cl-phenyl
1579	$-CH_2CH_2-$	bond	-O-	4-Cl-phenyl
1580	$-CH_2CH_2-$	bond	-O-	2-Me-phenyl
1581	$-CH_2CH_2-$	bond	-O-	3-Me-phenyl
1582	$-CH_2CH_2-$	bond	-O-	4-Me-phenyl
1583	$-CH_2CH_2-$	bond	-O-	2-MeO-phenyl
1584	$-CH_2CH_2-$	bond	-O-	3-MeO-phenyl
1585	$-CH_2CH_2-$	bond	-O-	4-MeO-phenyl
1586	$-CH_2CH_2-$	bond	-O-	2-MeS-phenyl
1587	$-CH_2CH_2-$	bond	-O-	3-MeS-phenyl
1588	$-CH_2CH_2-$	bond	-O-	4-MeS-phenyl
1589	$-CH_2CH_2-$	bond	-O-	2-F_3C-phenyl
1590	$-CH_2CH_2-$	bond	-O-	3-F_3C-phenyl
1591	$-CH_2CH_2-$	bond	-O-	4-F_3C-phenyl
1592	$-CH_2CH_2-$	bond	-O-	2,3-diF-phenyl
1593	$-CH_2CH_2-$	bond	-O-	2,4-diF-phenyl
1594	$-CH_2CH_2-$	bond	-O-	2,5-diF-phenyl
1595	$-CH_2CH_2-$	bond	-O-	2,6-diF-phenyl
1596	$-CH_2CH_2-$	bond	-O-	3,4-diF-phenyl
1597	$-CH_2CH_2-$	bond	-O-	3,5-diF-phenyl
1598	$-CH_2CH_2-$	bond	-O-	2,3-diCl-phenyl

1599	$-CH_2CH_2-$	bond	-O-	2,4-diCl-phenyl
1600	$-CH_2CH_2-$	bond	-O-	2,5-diCl-phenyl
1601	$-CH_2CH_2-$	bond	-O-	2,6-diCl-phenyl
1602	$-CH_2CH_2-$	bond	-O-	3,4-diCl-phenyl
1603	$-CH_2CH_2-$	bond	-O-	3,5-diCl-phenyl
1604	$-CH_2CH_2-$	bond	-O-	2-Cl-3-F-phenyl
1605	$-CH_2CH_2-$	bond	-O-	2-Cl-4-F-phenyl
1606	$-CH_2CH_2-$	bond	-O-	2-Cl-5-F-phenyl
1607	$-CH_2CH_2-$	bond	-O-	3-Cl-4-F-phenyl
1608	$-CH_2CH_2-$	bond	-O-	3-Cl-5-F-phenyl
1609	$-CH_2CH_2-$	bond	-O-	4-Cl-2-F-phenyl
1610	$-CH_2CH_2-$	bond	-O-	4-Cl-3-F-phenyl
1611	$-CH_2CH_2-$	bond	-O-	2,3-diMeO-phenyl
1612	$-CH_2CH_2-$	bond	-O-	2,4-diMeO-phenyl
1613	$-CH_2CH_2-$	bond	-O-	2,5-diMeO-phenyl
1614	$-CH_2CH_2-$	bond	-O-	2,6-diMeO-phenyl
1615	$-CH_2CH_2-$	bond	-O-	3,4-diMeO-phenyl
1616	$-CH_2CH_2-$	bond	-O-	3,5-diMeO-phenyl
1617	$-CH_2CH_2-$	bond	-O-	cyclopropyl
1618	$-CH_2CH_2-$	bond	-O-	cyclobutyl
1619	$-CH_2CH_2-$	bond	-O-	cyclopentyl
1620	$-CH_2CH_2-$	bond	-O-	cyclohexyl
1621	$-CH_2CH_2-$	bond	-O-	2-furanyl
1622	$-CH_2CH_2-$	bond	-O-	2-thienyl
1623	$-CH_2CH_2-$	bond	-O-	2-pyridyl
1624	$-CH_2CH_2-$	bond	-O-	3-pyridyl
1625	$-CH_2CH_2-$	bond	-O-	4-pyridyl
1626	$-CH_2CH_2-$	bond	-O-	3-Me-2-pyridyl
1627	$-CH_2CH_2-$	bond	-O-	4-Me-2-pyridyl
1628	$-CH_2CH_2-$	bond	-O-	2-benzothienyl
1629	$-CH_2CH_2-$	bond	-O-	2-benzofuranyl
1630	$-CH_2CH_2-$	bond	-O-	2-naphthyl
1631	$-CH_2CH_2CH_2-$	bond	-O-	phenyl
1632	$-CH_2CH_2CH_2-$	bond	-O-	3,3-diphenylmethyl

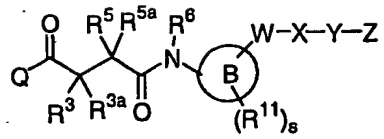
1633	$-CH_2CH_2CH_2-$	bond	-O-	2-F-phenyl
1634	$-CH_2CH_2CH_2-$	bond	-O-	3-F-phenyl
1635	$-CH_2CH_2CH_2-$	bond	-O-	4-F-phenyl
1636	$-CH_2CH_2CH_2-$	bond	-O-	2-Cl-phenyl
1637	$-CH_2CH_2CH_2-$	bond	-O-	3-Cl-phenyl
1638	$-CH_2CH_2CH_2-$	bond	-O-	4-Cl-phenyl
1639	$-CH_2CH_2CH_2-$	bond	-O-	2-Me-phenyl
1640	$-CH_2CH_2CH_2-$	bond	-O-	3-Me-phenyl
1641	$-CH_2CH_2CH_2-$	bond	-O-	4-Me-phenyl
1642	$-CH_2CH_2CH_2-$	bond	-O-	2-MeO-phenyl
1643	$-CH_2CH_2CH_2-$	bond	-O-	3-MeO-phenyl
1644	$-CH_2CH_2CH_2-$	bond	-O-	4-MeO-phenyl
1645	$-CH_2CH_2CH_2-$	bond	-O-	2-MeS-phenyl
1646	$-CH_2CH_2CH_2-$	bond	-O-	3-MeS-phenyl
1647	$-CH_2CH_2CH_2-$	bond	-O-	4-MeS-phenyl
1648	$-CH_2CH_2CH_2-$	bond	-O-	2-F_3C-phenyl
1649	$-CH_2CH_2CH_2-$	bond	-O-	3-F_3C-phenyl
1650	$-CH_2CH_2CH_2-$	bond	-O-	4-F_3C-phenyl
1651	$-CH_2CH_2CH_2-$	bond	-O-	2,3-diF-phenyl
1652	$-CH_2CH_2CH_2-$	bond	-O-	2,4-diF-phenyl
1653	$-CH_2CH_2CH_2-$	bond	-O-	2,5-diF-phenyl
1654	$-CH_2CH_2CH_2-$	bond	-O-	2,6-diF-phenyl
1655	$-CH_2CH_2CH_2-$	bond	-O-	3,4-diF-phenyl
1656	$-CH_2CH_2CH_2-$	bond	-O-	3,5-diF-phenyl
1657	$-CH_2CH_2CH_2-$	bond	-O-	2,3-diCl-phenyl
1658	$-CH_2CH_2CH_2-$	bond	-O-	2,4-diCl-phenyl
1659	$-CH_2CH_2CH_2-$	bond	-O-	2,5-diCl-phenyl
1660	$-CH_2CH_2CH_2-$	bond	-O-	2,6-diCl-phenyl
1661	$-CH_2CH_2CH_2-$	bond	-O-	3,4-diCl-phenyl
1662	$-CH_2CH_2CH_2-$	bond	-O-	3,5-diCl-phenyl
1663	$-CH_2CH_2CH_2-$	bond	-O-	2-Cl-3-F-phenyl
1664	$-CH_2CH_2CH_2-$	bond	-O-	2-Cl-4-F-phenyl
1665	$-CH_2CH_2CH_2-$	bond	-O-	2-Cl-5-F-phenyl
1666	$-CH_2CH_2CH_2-$	bond	-O-	3-Cl-4-F-phenyl

1667	$-CH_2CH_2CH_2-$	bond	-O-	3-Cl-5-F-phenyl
1668	$-CH_2CH_2CH_2-$	bond	-O-	4-Cl-2-F-phenyl
1669	$-CH_2CH_2CH_2-$	bond	-O-	4-Cl-3-F-phenyl
1670	$-CH_2CH_2CH_2-$	bond	-O-	2,3-diMeO-phenyl
1671	$-CH_2CH_2CH_2-$	bond	-O-	2,4-diMeO-phenyl
1672	$-CH_2CH_2CH_2-$	bond	-O-	2,5-diMeO-phenyl
1673	$-CH_2CH_2CH_2-$	bond	-O-	2,6-diMeO-phenyl
1674	$-CH_2CH_2CH_2-$	bond	-O-	3,4-diMeO-phenyl
1675	$-CH_2CH_2CH_2-$	bond	-O-	3,5-diMeO-phenyl
1676	$-CH_2CH_2CH_2-$	bond	-O-	cyclopropyl
1677	$-CH_2CH_2CH_2-$	bond	-O-	cyclobutyl
1678	$-CH_2CH_2CH_2-$	bond	-O-	cyclopentyl
1679	$-CH_2CH_2CH_2-$	bond	-O-	cyclohexyl
1680	$-CH_2CH_2CH_2-$	bond	-O-	2-furanyl
1681	$-CH_2CH_2CH_2-$	bond	-O-	2-thienyl
1682	$-CH_2CH_2CH_2-$	bond	-O-	2-pyridyl
1683	$-CH_2CH_2CH_2-$	bond	-O-	3-pyridyl
1684	$-CH_2CH_2CH_2-$	bond	-O-	4-pyridyl
1685	$-CH_2CH_2CH_2-$	bond	-O-	3-Me-2-pyridyl
1686	$-CH_2CH_2CH_2-$	bond	-O-	4-Me-2-pyridyl
1687	$-CH_2CH_2CH_2-$	bond	-O-	2-benzothienyl
1688	$-CH_2CH_2CH_2-$	bond	-O-	2-benzofuranyl
1689	$-CH_2CH_2CH_2-$	bond	-O-	2-naphthyl

CLAIMS

What is claimed is:

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

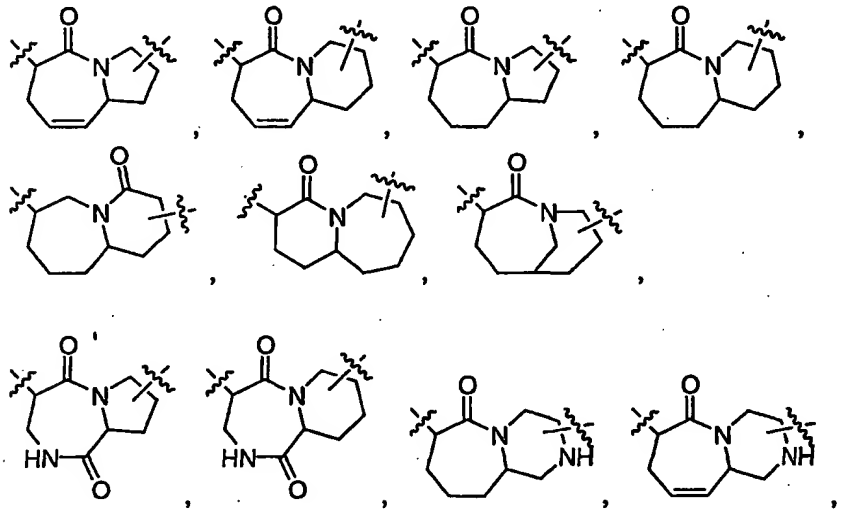
Q is $-OR^1$ or $-NR^1R^2$;

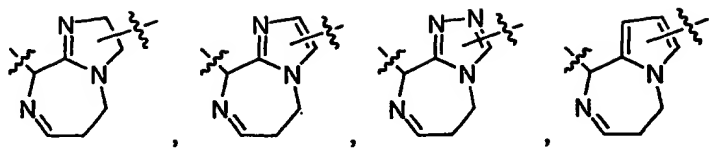
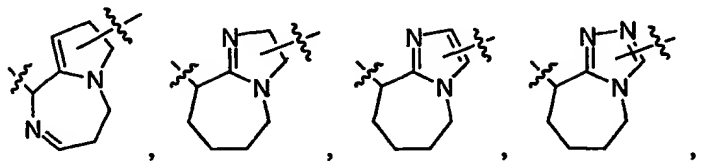
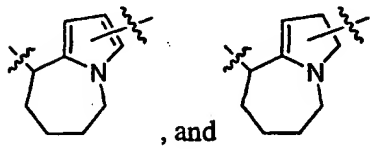
ring B is selected from the group consisting of:

a carbocyclic group of 3 to 8 carbon atoms wherein the carbocyclic group is saturated, partially saturated or unsaturated;

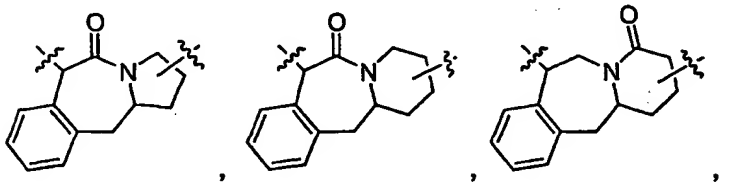
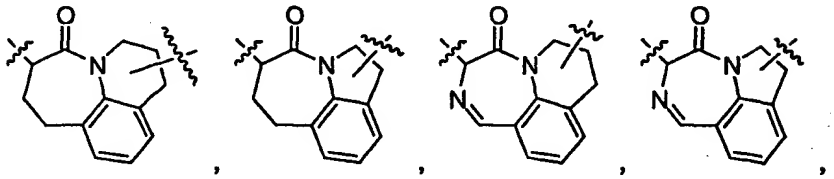
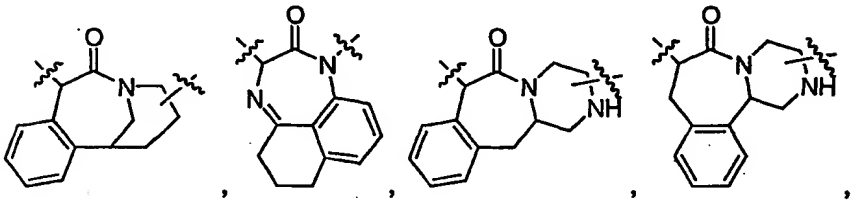
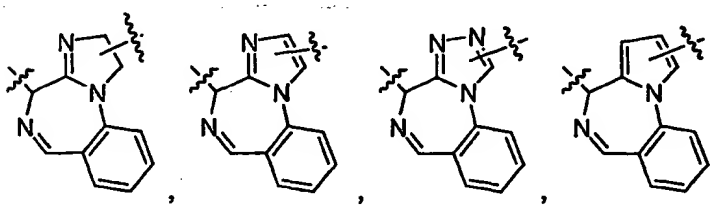
a heterocycle of 3 to 8 atoms containing a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, $-S(=O)_2-$, and $-N(R^{10})-$;

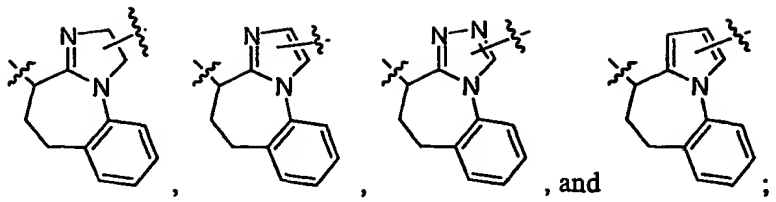
a bicyclic ring system selected from the group consisting of:






, and ;

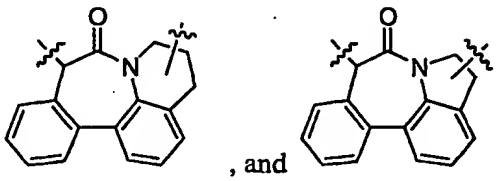
a tricyclic ring system selected from the group consisting of:





, ;



and

a tetracyclic ring system selected from the group consisting of:



s is 0, 1, 2, 3, 4, 5, or 6;

R^1, at each occurrence, is independently selected from:

H;

C_1-C_6 alkyl substituted with 0-3 R^{1a};

C_2-C_6 alkenyl substituted with 0-3 R^{1a};

C_3-C_{10} carbocycle substituted with 0-3 R^{1b};

C_6-C_{10} aryl substituted with 0-3 R^{1b}; and

5 to 10 membered heterocycle substituted with 0-3 R^{1b};

R^{1a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3;

C_3-C_{10} carbocycle substituted with 0-3 R^{1b};

C_6-C_{10} aryl substituted with 0-3 R^{1b}; and

5 to 6 membered heterocycle substituted with 0-3 R^{1b};

R^{1b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^2 is independently selected from H, NH_2, OH, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenoxy, benzyloxy, C_3-C_{10} carbocycle, C_6-C_{10} aryl and 5 to 10 membered heterocycle;

R^3 is $-(CR^7R^{7a})_n-R^4$,
$-(CR^7R^{7a})_n-S-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-O-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-S(=O)-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-S(=O)_2-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-C(=O)-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})C(=O)-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-C(=O)N(R^{7b})-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})S(=O)_2-(CR^7R^{7a})_m-R^4$, or
$-(CR^7R^{7a})_n-S(=O)_2N(R^{7b})-(CR^7R^{7a})_m-R^4$;

n is 0, 1, 2, or 3;

m is 0, 1, 2, or 3;

R^{3a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, or C_2-C_4 alkenyloxy;

alternatively, R^3 and R^{3a} may be combined to form a 3-7 membered carbocyclic moiety;
wherein said 3-7 membered carbocyclic moiety is saturated or partially unsaturated;
wherein said 3-7 membered carbocyclic moiety may optionally contain a heteroatom selected from -O-, -S-, -S(=O)-, $-S(=O)_2-$, -N=, -NH-, and $-N(R^{20})-$, and
wherein said 3-7 membered carbocyclic moiety is substituted with 0-4 R^4;

additionally, two R^4 substituents on adjacent atoms may be combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{23};

additionally, two R^4 substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R^{23};

additionally, two R^4 substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle substituted with 0-3 R^{23};

R^4 is H, OH, OR^{14a},

C_1-C_6 alkyl substituted with 0-3 R^{4a},
C_2-C_6 alkenyl substituted with 0-3 R^{4a},
C_2-C_6 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, Br, I, CF_3,
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^5 is H, OR^{14};
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_1-C_6 alkoxy substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3R^{5c};

R^{5a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_2-C_4 alkenyl, or C_2-C_4 alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^5 and R^{5a} may be combined to form a 3-7 membered carbocyclic ring substituted with 0-3 R^{5c}; optionally the carbocyclic ring formed by combining R^5 and R^{5a} may be benzo fused, wherein the benzo fused ring may be substituted with 0-3 R^{5c};

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^7, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, and C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, aryl and C_1-C_4 alkyl;

R^{7b} is independently selected from H and C_1-C_4 alkyl;

W is $-(CR^8R^{8a})_p-$;

p is 0, 1, 2, 3, or 4;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

Y is a bond or $-(CR^9R^{9a})_t$-V-$(CR^9R^{9a})_u$-;

t is 0, 1, 2, or 3;

u is 0, 1, 2, or 3;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, $-S(=O)_2$-, $-N(R^{19})$-, $-C(=O)NR^{19b}$-, $-NR^{19b}C(=O)$-, $-NR^{19b}S(=O)_2$-, $-S(=O)_2NR^{19b}$-, $-NR^{19b}S(=O)$-, $-S(=O)NR^{19b}$-, -C(=O)O-, or -OC(=O)-;

Z is H;

C_1-C_8 alkyl substituted with 0-3 R^{12a};

C_2-C_4 alkenyl substituted with 0-3 R^{12a};

C_2-C_4 alkynyl substituted with 0-3 R^{12a};

C_6-C_{10} aryl substituted with 0-4 R^{12a};

C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or

5 to 10 membered heterocycle substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,

C_1-C_3 alkyl substituted with 0-1 R^{12c};

C_6-C_{10} aryl substituted with 0-4 R^{12b};

C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{12c}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl substituted with 0-2 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^{10} may be -W-X-Y-Z;

R^{11}, at each occurrence, is independently selected from
H, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl substituted with 0-1 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{13};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14}, at each occurrence, is independently selected from H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{17} is H, aryl, aryl-CH_2-, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring;

R^{20} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl optionally substituted with 0-3 R^{20a}; or

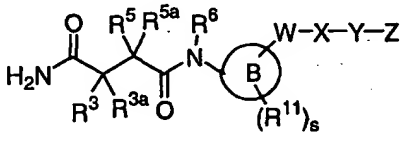
C_6-C_{10} aryl substituted with 0-4 R^{20b};

R^{20a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{20b};

R^{20b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{23}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3.

2. A compound of Claim 1 of Formula (Ia):



(Ia)

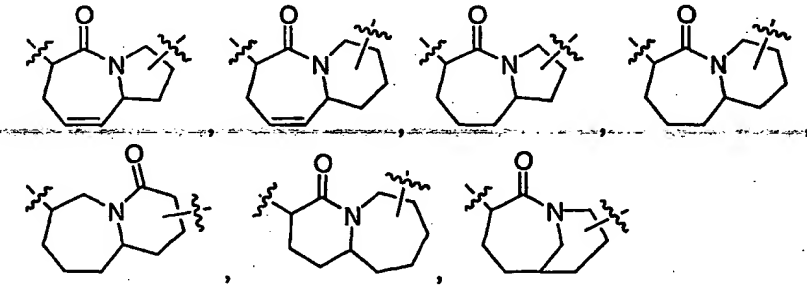
or a pharmaceutically acceptable salt or prodrug thereof, wherein:

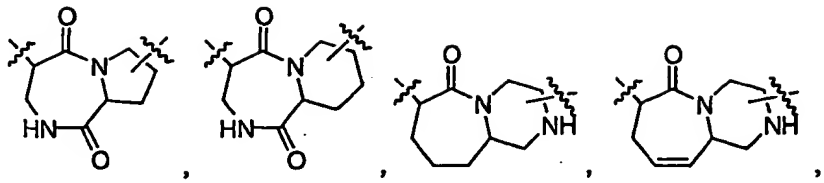
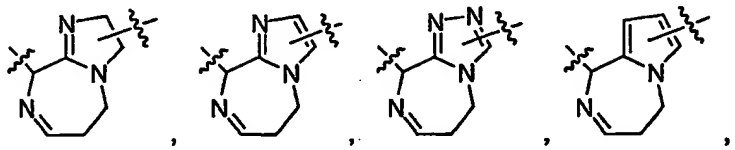
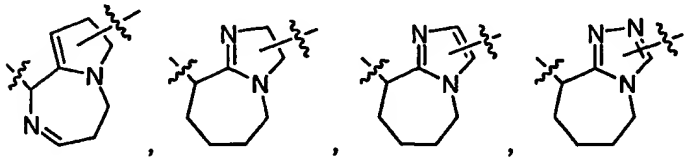
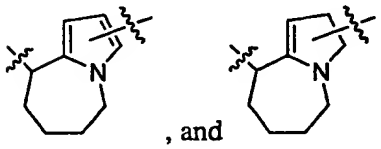
ring B is selected from the group consisting of:

a carbocyclic group of 5 to 7 carbon atoms wherein the carbocyclic group is saturated, partially saturated or unsaturated;

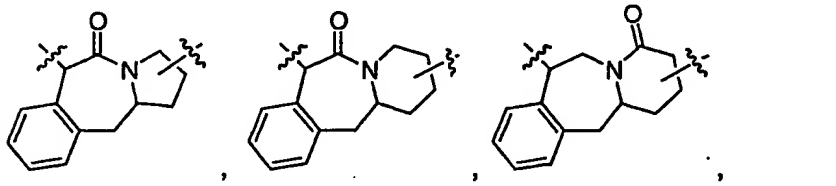
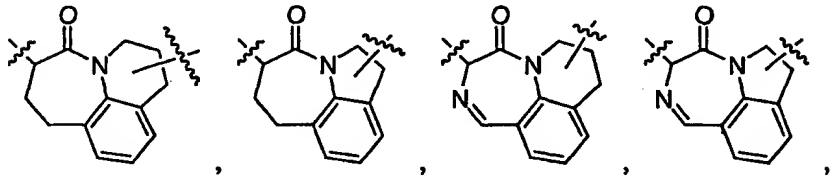
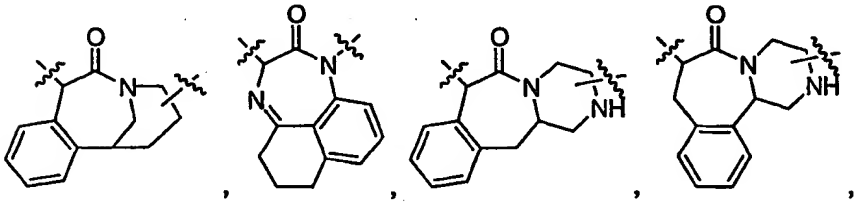
a heterocycle of 5 to 7 atoms containing a heteroatom selected from the group consisting of -O-, -S-, -S(=O)-, -$S(=O)_2$-, and -$N(R^{10})$-;

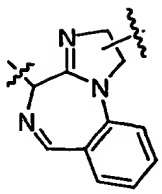
a bicyclic ring system selected from the group consisting of:







, and ;

a tricyclic ring system selected from the group consisting of: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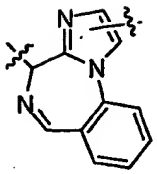
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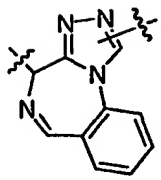
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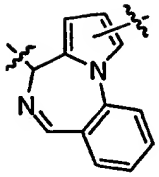
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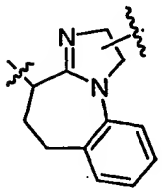
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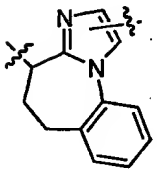
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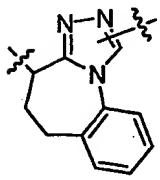
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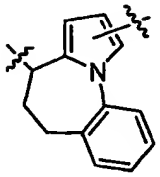
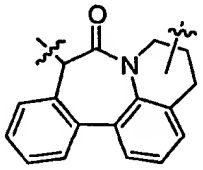

;

and

a tetracyclic ring system selected from the group consisting of: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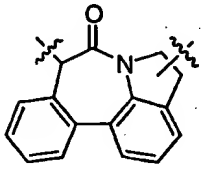


s is 0, 1, 2, 3, or 4;

R^3 is $-(CR^7R^{7a})_n-R^4$,
$-(CR^7R^{7a})_n-S-R^4$,
$-(CR^7R^{7a})_n-O-R^4$,
$-(CR^7R^{7a})_n-N(R^{7b})-R^4$,
$-(CR^7R^{7a})_n-S(=O)-R^4$,
$-(CR^7R^{7a})_n-S(=O)_2-R^4$, or
$-(CR^7R^{7a})_n-C(=O)-R^4$;

n is 0, 1, or 2;

R^{3a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, or C_2-C_4 alkenyloxy;

alternatively, R^3 and R^{3a} may be combined to form a 3-7 membered carbocyclic moiety; wherein said 3-7 membered carbocyclic moiety is saturated or partially unsaturated;

wherein said 3-7 membered carbocyclic moiety may optionally contain a heteroatom selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, -N=, -NH-, and -N(R^{20})-, and

wherein said 3-7 membered carbocyclic moiety is substituted with 0-4 R^4;

additionally, two R^4 substituents on adjacent atoms may be combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{23};

additionally, two R^4 substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R^{23};

additionally, two R^4 substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle substituted with 0-3 R^{23};

R^4 is H, OH, OR^{14a},

C_1-C_6 alkyl substituted with 0-3 R^{4a},

C_2-C_6 alkenyl substituted with 0-3 R^{4a},

C_2-C_6 alkynyl substituted with 0-3 R^{4a},

C_3-C_{10} carbocycle substituted with 0-3 R^{4b},

C_6-C_{10} aryl substituted with 0-3 R^{4b}, or

5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, Br, I, CF_3,

C_3-C_{10} carbocycle substituted with 0-3 R^{4b},

C_6-C_{10} aryl substituted with 0-3 R^{4b}, or

5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, S(=O)CH_3, S(=O)$_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^5 is H;

C_1-C_6 alkyl substituted with 0-3 R^{5b};

C_2-C_6 alkenyl substituted with 0-3 R^{5b};

C_2-C_6 alkynyl substituted with 0-3 R^{5b};

C_3-C_{10} carbocycle substituted with 0-3 R^{5c}; or

C_6-C_{10} aryl substituted with 0-3 R^{5c};

R^{5a} is H, C_1-C_4 alkyl, or C_2-C_4 alkenyl;

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^5 and R^{5a} may be combined to form a 3-7 membered carbocyclic ring substituted with 0-3 R^{5c}; optionally the carbocyclic ring formed by combining R^5 and R^{5a} may be benzo fused, wherein the benzo fused ring may be substituted with 0-3 R^{5c};

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^7, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, and C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, aryl and C_1-C_4 alkyl;

R^{7b} is independently selected from H and C_1-C_4 alkyl;

W is $-(CR^8R^{8a})_p-$;

p is 0, 1, 2, or 3;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

Y is a bond or $-(CR^9R^{9a})_t-V-(CR^9R^{9a})_u-$;

t is 0, 1, 2, or 3;

u is 0, 1, 2, or 3;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a};
C_2-C_4 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12a};
C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12a}; or

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_1-C_3 alkyl substituted with 0-1 R^{12c};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^{12c}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl substituted with 0-2 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$,

$S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

alternatively, R^{10} may be -W-X-Y-Z;

R^{11}, at each occurrence, is independently selected from H,
C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl substituted with 0-1 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{13};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14}, at each occurrence, is independently selected from H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{17} is H, aryl, aryl-CH_2-, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring;

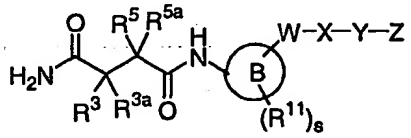
R^{20} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$,
$S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl optionally substituted with 0-3 R^{20a}; or
C_6-C_{10} aryl substituted with 0-4 R^{20b};

R^{20a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{20b};

R^{20b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{23}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3.

3. A compound of Claim 2 of Formula (Ia):

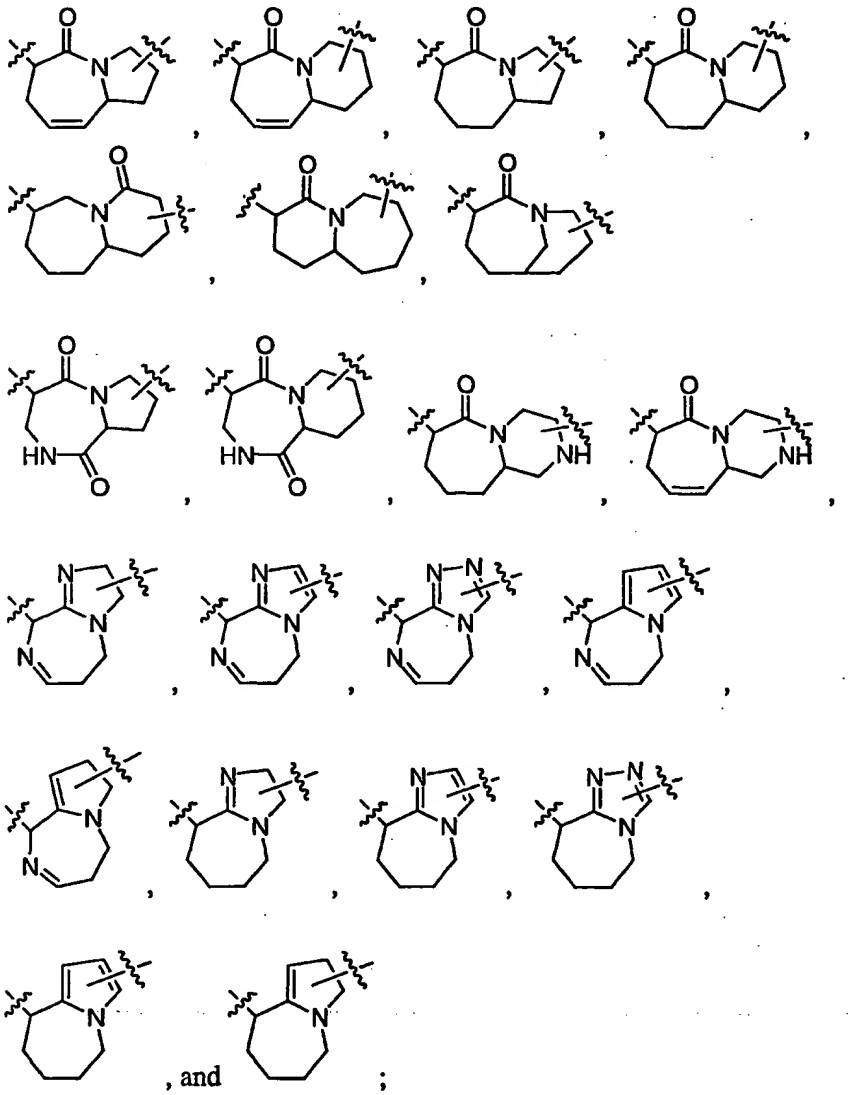


(Ia)

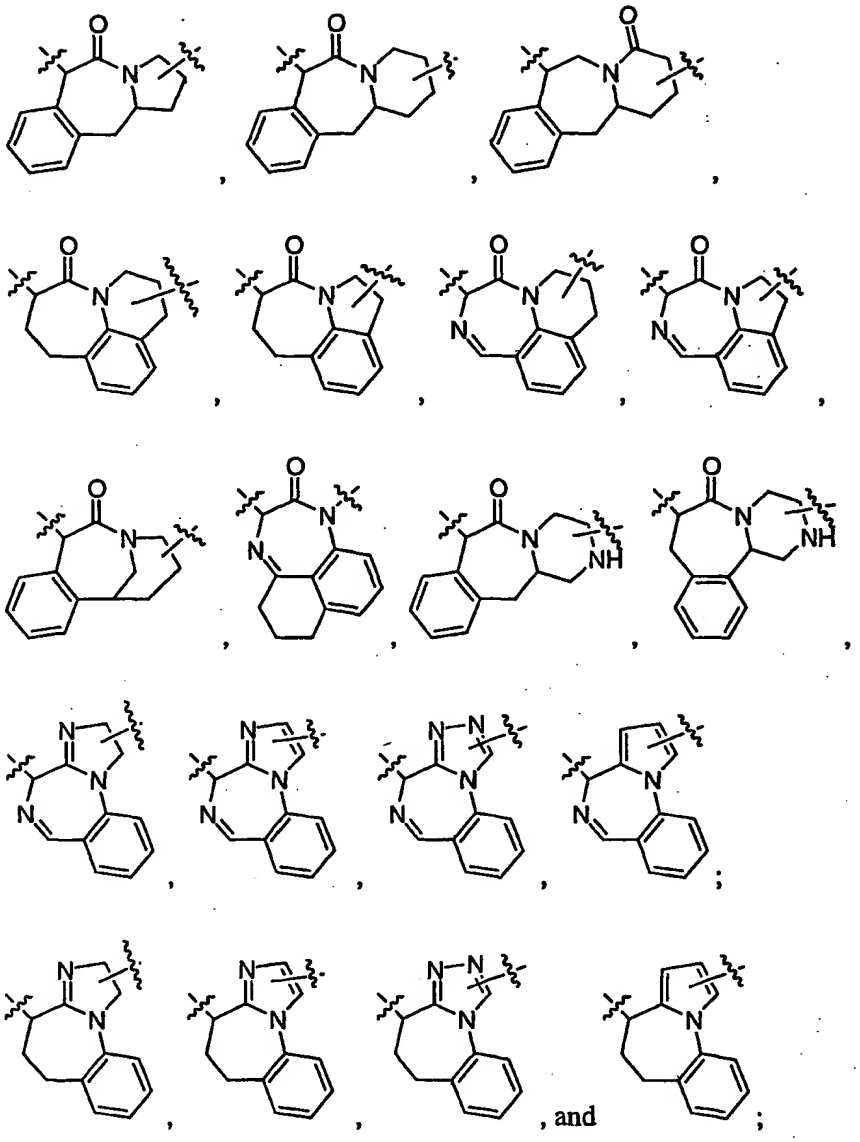
or a pharmaceutically acceptable salt or prodrug thereof, wherein:

ring B is selected from the group consisting of:

a carbocyclic group of 5, 6, or 7 carbon atoms selected from
-cyclopentylene-, -cyclohexylene-, -cycloheptylene-, -cyclopentenylene-, -cyclohexenylene-, and -phenylene-;
a heterocycle of 5, 6, or 7 atoms selected from
-pyrrolidinylene-, -piperidinylene-, -homopiperidinylene-, and -thiophenylene-;
a bicyclic ring system selected from the group consisting of:

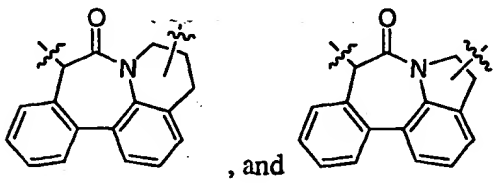


a tricyclic ring system selected from the group consisting of:



and

a tetracyclic ring system selected from the group consisting of:



s is 0, 1, 2, 3, or 4;

R^3 is $-(CH_2)_n-R^4$;

n is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, or butoxy;

alternatively, R^3 and R^{3a} may be combined to form a 3-7 membered carbocyclic moiety;
wherein said 3-7 membered carbocyclic moiety is saturated or partially unsaturated;
wherein said 3-7 membered carbocyclic moiety is substituted with 0-2 R^4;

R^4 is H, OH,
C_1-C_4 alkyl substituted with 0-2 R^{4a},
C_2-C_4 alkenyl substituted with 0-2 R^{4a},
C_2-C_4 alkynyl substituted with 0-1 R^{4a},
C_3-C_6 cycloklyl substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, CF_3,
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^5 is H;
C_1-C_4 alkyl substituted with 0-2 R^{5b};
C_2-C_4 alkenyl substituted with 0-2 R^{5b};
C_2-C_4 alkynyl substituted with 0-2 R^{5b};
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c}; or
phenyl substituted with 0-3 R^{5c};

R^{5a} is H, methyl, ethyl, propyl, butyl, or allyl;

R^{5b}, at each occurrence, is independently selected from:

H, methyl, ethyl, propyl, butyl, CF_3, OR^{14},
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle substituted with 0-2 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

alternatively, R^5 and R^{5a} may be combined to form a 3-7 membered carbocyclic ring substituted with 0-3 R^{5c};

W is a bond, $-CH_2-$, $-CH(CH_3)-$, $-CH_2CH_2-$ or $-CH(CH_3)CH_2-$;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-2 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Y is a bond, $-CH_2CH_2-V-$, $-CH_2-V-$, or $-V-$;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a};
C_2-C_4 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12a};
C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12a}; or

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_1-C_3 alkyl substituted with 0-1 R^{12c};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{12c}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{11}, at each occurrence, is independently selected from H,
C_1-C_4 alkoxy, Cl, F, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF_3;
C_1-C_4 alkyl substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{17} is H, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-methylphenyl, 4-trifluorophenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-methylphenyl)methyl, (4-trifluorophenyl)methyl, methyl, ethyl, propyl, butyl, methoxymethyl, methyoxyethyl, ethoxymethyl, or ethoxyethyl;

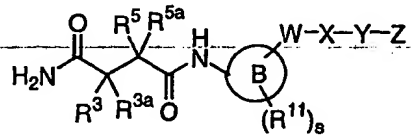
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl;

R^{19b} is H, mehyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring.

4. A compound of Claim 3 of Formula (Ia):

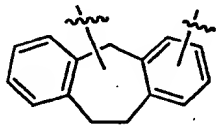


(Ia)

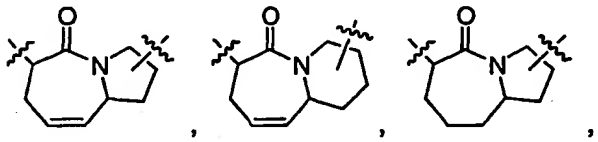
or a pharmaceutically acceptable salt or prodrug thereof, wherein:

ring B is selected from the group consisting of:

-cyclopent-1,2-diyl-, -cyclopent-1,3-diyl-, -cyclohex-1,2-diyl-, -cyclohex-1,3-diyl-, -cyclohex-1,4-diyl-, -cyclohept-1,3-diyl-, -cyclopenten-3,5-diyl-, -phen-1,2-diyl-, -phen-1,3-diyl-, -phen-1,4-diyl-, -pyrrolidin-1,4-diyl-, -pyrrolidin-2,4-diyl-, -piperidin-1,4-diyl-, -piperidin-1,3-diyl-, -thiophen-2,3-diyl-, and


;

a bicyclic ring system selected from the group consisting of: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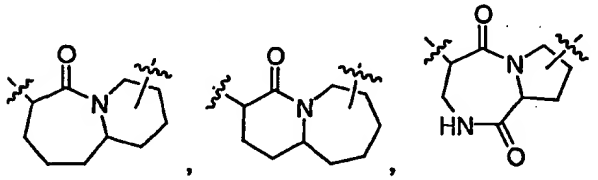
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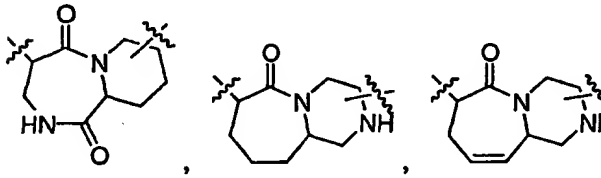
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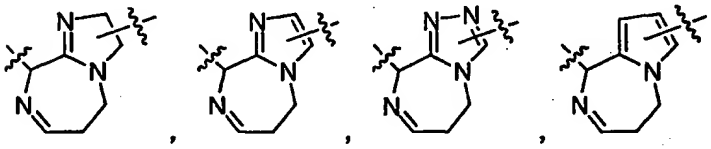
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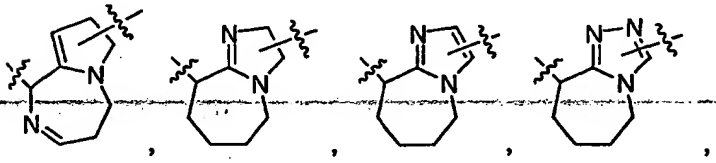
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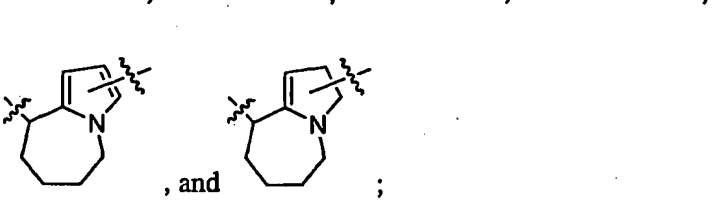
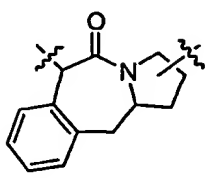

, and ;

a tricyclic ring system selected from the group consisting of: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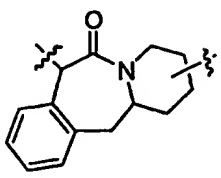
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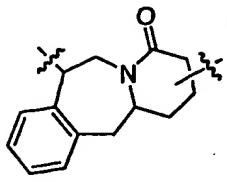
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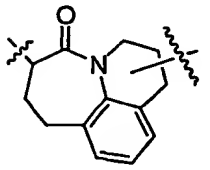
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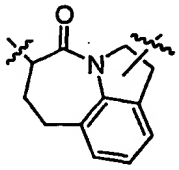
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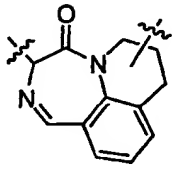
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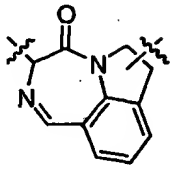
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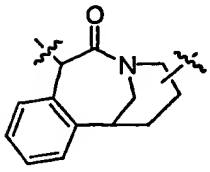
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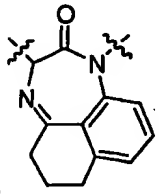
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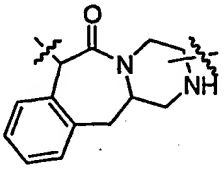
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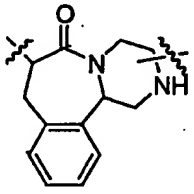
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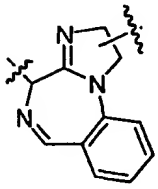
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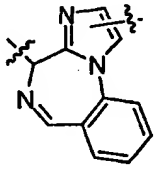
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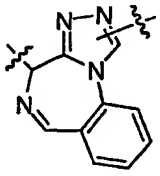
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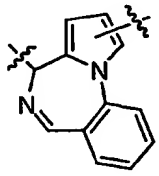
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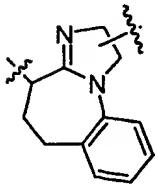
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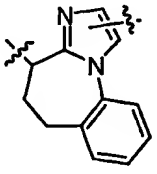
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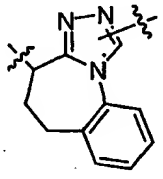
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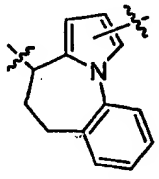
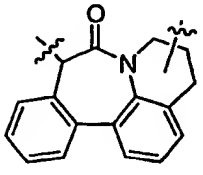

;

and

a tetracyclic ring system selected from the group consisting of: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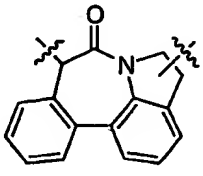


s is 0, 1, or 2;

R^3 is $-R^4$, $-CH_2-R^4$, or $-CH_2CH_2-R^4$;

R^{3a} is H;

alternatively, R^3 and R^{3a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl moiety;

R^4 is H, C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_2-C_4 alkynyl;

R^5 is C_1-C_4 alkyl substituted with 0-1 R^{5b};
C_2-C_4 alkenyl substituted with 0-1 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-1 R^{5b};

R^{5a} is H;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, OR^{14},
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle substituted with 0-2 R^{5c};

alternatively, R^5 and R^{5a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl ring;

W is a bond, $-CH_2-$, $-CH(CH_3)-$, $-CH_2CH_2-$ or $-CH(CH_3)CH_2-$;

X is a bond, phenyl, pyridyl, cyclopentyl, cyclohexyl, piperidinyl, or pyrrolidinyl;

Y is a bond, $-CH_2CH_2-V-$, $-CH_2-V-$, or $-V-$;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a};

C_2-C_4 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-2 R^{12a};
C_3-C_{10} carbocycle substituted with 0-4 R^{12a}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12a}; or

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, -C(=O)$NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_1-C_3 alkyl substituted with 0-1 R^{12c};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{12c}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{11}, at each occurrence, is independently selected from
H, C_1-C_4 alkoxy, Cl, F, =O, $NR^{18}R^{19}$, C(=O)R^{17}, C(=O)OR^{17}, CF_3;
C_1-C_4 alkyl substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_4 alkyl) and -S(=O)$_2$-(C_1-C_4 alkyl);

R^{17} is H, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-methylphenyl, 4-trifluorophenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-methylphenyl)methyl, (4-trifluorophenyl)methyl, methyl, ethyl, propyl, butyl, methoxymethyl, methyoxyethyl, ethoxymethyl, or ethoxyethyl;

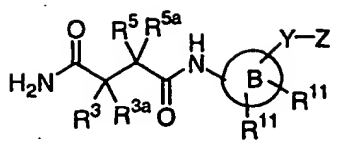
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl;

R^{19b} is H, mehyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring.

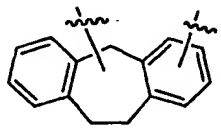
5. A compound of Claim 4 of Formula (Ic):

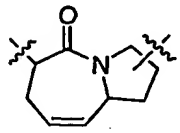
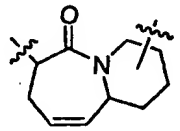
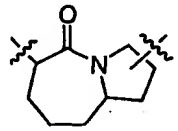
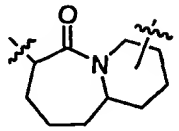


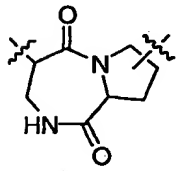
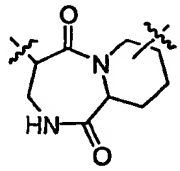
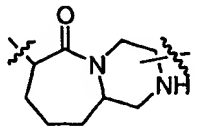
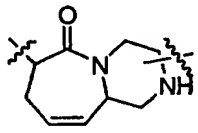
(Ic)

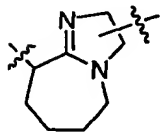
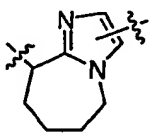
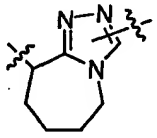
or a pharmaceutically acceptable salt or prodrug thereof, wherein:

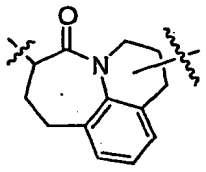
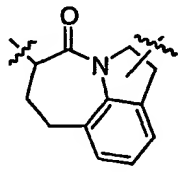
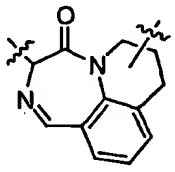
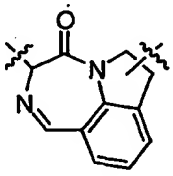
ring B is selected from the group consisting of:

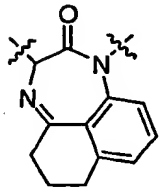
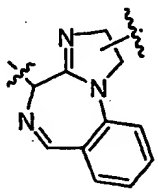
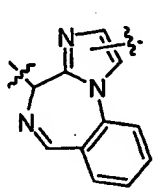
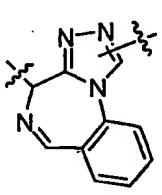
 ,

 ,  ,  ,  ,

 ,  ,  ,  ,

 ,  ,  ;

 ,  ,  ,  ,

 ,  ,  , and  ,

R^3 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_3$,

$-CH_2(CH_3)_2$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, $-CH=CH_2$, $-CH_2CH=CH_2$, $-CH_2C(CH_3)=CH_2$, $-CH_2CH=C(CH_3)_2$, $-CH_2CH_2CH=CH_2$, $-CH_2CH_2C(CH_3)=CH_2$, $-CH_2CH_2CH=C(CH_3)_2$, cis-$CH_2CH=CH(CH_3)$, cis-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(CH_3)$, trans-$CH_2CH_2CH=CH(CH_3)$, $-C\equiv CH$, $-CH_2C\equiv CH$, or $-CH_2C\equiv C(CH_3)$;

R^{3a} is H;

alternatively, R^3 and R^{3a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl moiety;

R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_2CH_3$, $-CH_2CH(CH_3)CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH(CH_2CH_3)_2$, $-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$, cis-$CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(CH_3)$, $-CH_2CH=C(CH_3)_2$, cis-$CH_2CH=CHCH_2CH_3$, trans-$CH_2CH=CHCH_2CH_3$, cis-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH_2CH=CH(CH_3)$, $-C\equiv CH$, $-CH_2C\equiv CH$, $-CH_2C\equiv C(CH_3)$, $-CH_2CH_2C\equiv CH$, or $-CH_2CH_2C\equiv C(CH_3)$;

R^{5a} is H;

alternatively, R^5 and R^{5a} may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl ring;

Y is a bond, $-CH_2CH_2$-V-, $-CH_2$-V-, or -V-;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, $-S(=O)_2$-, $-N(R^{19})$-, $-C(=O)NR^{19b}$-, $-NR^{19b}C(=O)$-, -C(=O)O-, or -OC(=O)-;

Z is H;

C_1-C_4 alkyl substituted with 0-1 R^{12a};

C_2-C_4 alkenyl substituted with 0-1 R^{12a};

C_2-C_4 alkynyl substituted with 0-1 R^{12a};

phenyl substituted with 0-2 R^{12a};

C_3-C_6 cycloalkyl, selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; substituted with 0-2 R^{12a}; or

5 to 10 membered heterocycle selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrrolidinyl, piperidinyl, N-piperinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, morpholinyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl; wherein said 5 to 10 membered heterocycle is substituted with 0-2 R^{12a};

R^{12a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, CN, NO_2, $NR^{15}R^{16}$, -C(=O)$NR^{15}R^{16}$, CF_3, acetyl, SCH_3, SCF_3, S(=O)CH_3, S(=O)$_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, C_1-C_2 haloalkyl, C_1-C_2 haloalkoxy,

C_1-C_3 alkyl substituted with R^{12c};

phenyl substituted with 0-3 R^{12b};

5 to 10 membered heterocycle selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrrolidinyl, piperidinyl, N-piperinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, morpholinyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl; wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, S(=O)CH_3, S(=O)$_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{12c}, at each occurrence, is independently selected from

phenyl substituted with 0-4 R^{12b};

C_3-C_{10} cycloalkyl, selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrrolidinyl, piperidinyl, N-piperinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, morpholinyl, benzofuranyl, benzothiofuranyl, indolyl,

benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl; wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{11}, at each occurrence, is independently selected from H, Cl, F, $NR^{18}R^{19}$, methyl, ethyl, methoxy, ethoxy, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, or (4-CF_3-phenyl)CH_2CH_2-; and

R^{15}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, propyl-C(=O)-, butyl-C(=O)-, methyl-$S(=O)_2$-, ethyl- $S(=O)_2$-, propyl-$S(=O)_2$-, and butyl-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, propyl-C(=O)-, butyl-C(=O)-, methyl-$S(=O)_2$-, ethyl- $S(=O)_2$-, propyl-$S(=O)_2$-, and butyl-$S(=O)_2$-;

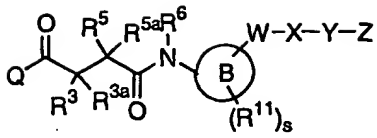
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl;

R^{19b} is H, mehyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, phenyl, benzyl or phenethyl;

additionally, R^{18} and R^{19}, when substituents on the same atom, may be combined to form a 3 to 7 membered heterocyclic ring selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, and morpholinyl.

6. A compound of Claim 1 of Formula (I):

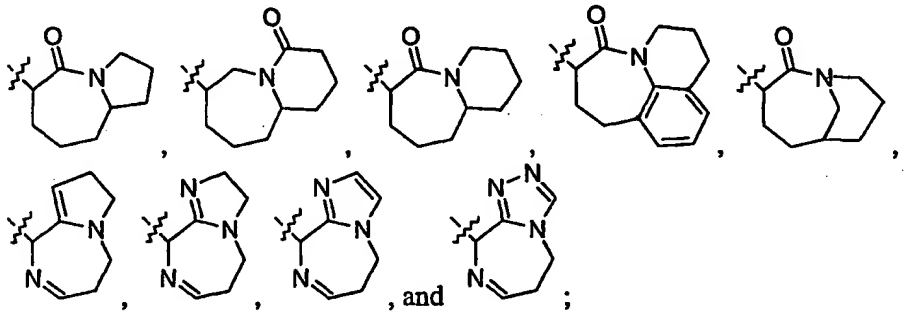


(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is NH_2;

ring B is cycloalkyl group of 3 to 8 carbon atoms wherein the cycloalkyl group is saturated, partially saturated or unsaturated; a heterocycle of 3 to 8 atoms containing a heteroatom selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, and -N(R^{10})-;



s is 0, 1, 2, 3, 4, 5, or 6;

R^3 is -(CR^7R^{7a})$_n$-R^4,
-(CR^7R^{7a})$_n$-S-(CR^7R^{7a})$_m$-R^4,
-(CR^7R^{7a})$_n$-O-(CR^7R^{7a})$_m$-R^4, or
-(CR^7R^{7a})$_n$-N(R^{7b})-(CR^7R^{7a})$_m$-R^4;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, or butoxy;

R^4 is H, OH, OR^{14a},
C_1-C_4 alkyl substituted with 0-2 R^{4a},
C_2-C_4 alkenyl substituted with 0-2 R^{4a},
C_2-C_4 alkynyl substituted with 0-2 R^{4a},

C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, Br, I CF_3,
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^5 is H, OR^{14};
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3R^{5c};

R^{5a} is H, OH, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_2-C_4 alkenyl, or C_2-C_4 alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^6 is H, methyl, or ethyl;

R^7, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, and C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, CF_3, phenyl and C_1-C_4 alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

W is $-(CR^8R^{8a})_p-$;

p is 0, 1, or 2;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl and C_3-C_6 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-2 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

Y is a bond or $-(CR^9R^{9a})_t$-V-$(CR^9R^{9a})_u-$;

t is 0, 1, or 2;

u is 0, 1, or 2;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl or C_3-C_6 cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, or $-S(=O)NR^{19b}-$;

Z is C_1-C_3 alkyl substituted with 1-2 R^{12};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12} is C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl substituted with 0-1 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{11}, at each occurrence, is independently selected from
C_1-C_4 alkoxy, Cl, F, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl substituted with 0-1 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl);

R^{17} is H, aryl, (aryl)CH_2-, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -$S(=O)_2$-(C_1-C_6 alkyl); and

R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl.

7. A compound of Claim 6 wherein:

R^3 is -$(CR^7R^{7a})_n$-R^4,
-$(CR^7R^{7a})_n$-S-$(CR^7R^{7a})_m$-R^4,
-$(CR^7R^{7a})_n$-O-$(CR^7R^{7a})_m$-R^4, or
-$(CR^7R^{7a})_n$-$N(R^{7b})$-$(CR^7R^{7a})_m$-R^4;

n is 0 or 1;

m is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, or butoxy;

R^4 is H, OH,
C_1-C_4 alkyl substituted with 0-2 R^{4a},
C_2-C_4 alkenyl substituted with 0-2 R^{4a},
C_2-C_4 alkynyl substituted with 0-1 R^{4a},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or

5 to 10 membered heterocycle substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, F, Cl, CF_3,
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^5 is H, OR^{14};
C_1-C_4 alkyl substituted with 0-3 R^{5b};
C_2-C_4 alkenyl substituted with 0-2 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-2 R^{5b};

R^{5a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, or allyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, OR^{14}, =O;
C_3-C_6 cycloalkyl substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle substituted with 0-2 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^6 is H;

R^7, at each occurrence, is independently selected from H, F, CF_3, methyl, and ethyl;

R^{7a}, at each occurrence, is independently selected from H, F, CF_3, methyl, and ethyl;

R^{7b} is independently selected from H, methyl, and ethyl;

W is a bond, $-CH_2-$, $-CH(CH_3)-$, $-CH_2CH_2-$ or $-CH(CH_3)CH_2-$;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-2 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Y is a bond, $-CH_2-V-$, $-V-$, or $-V-CH_2-$;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, or $-N(CH_2CH_3)-$,

Z is C_1-C_2 alkyl substituted with 1-2 R^{12};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_6 carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12} is C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_6 carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$;
C_1-C_4 alkyl substituted with 0-1 R^{10a};
phenyl substituted with 0-4 R^{10b};
C_3-C_6 carbocycle substituted with 0-3 R^{10b}; or
5 to 6 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, C_1-C_3 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{11}, at each occurrence, is independently selected from
C_1-C_4 alkoxy, Cl, F, =O, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF_3;
C_1-C_4 alkyl substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, benzyl, phenethyl, $-C(=O)-(C_1$-C_4 alkyl) and $-S(=O)_2-(C_1$-C_4 alkyl);

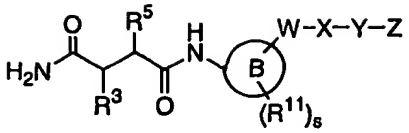
R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_4 alkyl, benzyl, phenethyl, $-C(=O)-(C_1$-C_4 alkyl) and $-S(=O)_2-(C_1$-C_4 alkyl);

R^{17} is H, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-methylphenyl, 4-trifluorophenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-methylphenyl)methyl, (4-trifluorophenyl)methyl, methyl, ethyl, propyl, butyl, methoxymethyl, methyoxyethyl, ethoxymethyl, or ethoxyethyl;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, and ethyl.

8. A compound of Claim 7 of Formula (Ib) wherein:



(Ib)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

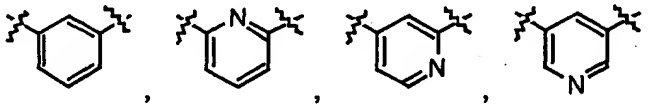
R^3 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_3$, $-CH_2(CH_3)_2$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, $-CF_3$, $-CH_2CF_3$, $-CH_2CH_2CF_3$, $-CH_2CH_2CH_2CF_3$, $-CH=CH_2$, $-CH_2CH=CH_2$, $-CH_2C(CH_3)=CH_2$, $-CH_2CH=C(CH_3)_2$, $-CH_2CH_2CH=CH_2$, $-CH_2CH_2C(CH_3)=CH_2$, $-CH_2CH_2CH=C(CH_3)_2$, cis-$CH_2CH=CH(CH_3)$, cis-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(CH_3)$, trans-$CH_2CH_2CH=CH(CH_3)$; $-C\equiv CH$, $-CH_2C\equiv CH$, $-CH_2C\equiv C(CH_3)$, cyclopropyl-CH_2-, cyclobutyl-CH_2-, cyclopentyl-CH_2-, cyclohexyl-CH_2-, cyclopropyl-CH_2CH_2-, cyclobutyl-CH_2CH_2-, cyclopentyl-CH_2CH_2-, cyclohexyl-CH_2CH_2-, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-, (3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, phenyl-CH_2CH_2-, (2-F-phenyl)CH_2CH_2-, (3-F-phenyl)CH_2CH_2-, (4-F-phenyl)CH_2CH_2-, (2-Cl-phenyl)CH_2CH_2-, (3-Cl-phenyl)CH_2CH_2-, (4-Cl-phenyl)CH_2CH_2-, (2,3-diF-phenyl)CH_2CH_2-, (2,4-diF-phenyl)CH_2CH_2-, (2,5-diF-phenyl)CH_2CH_2-, (2,6-diF-phenyl)CH_2CH_2-, (3,4-diF-phenyl)CH_2CH_2-, (3,5-diF-phenyl)CH_2CH_2-, (2,3-diCl-phenyl)CH_2CH_2-, (2,4-diCl-phenyl)CH_2CH_2-, (2,5-diCl-phenyl)CH_2CH_2-, (2,6-diCl-phenyl)CH_2CH_2-, (3,4-diCl-phenyl)CH_2CH_2-, (3,5-diCl-phenyl)CH_2CH_2-, (3-F-4-Cl-phenyl)CH_2CH_2-, or (3-F-5-Cl-phenyl)CH_2CH_2-;

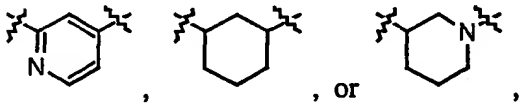
R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_2CH_3$, $-CH_2CH(CH_3)CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$,

-$CH(CH_2CH_3)_2$, -CF_3, -CH_2CF_3, -$CH_2CH_2CF_3$, -$CH_2CH_2CH_2CF_3$, -$CH_2CH_2CH_2CH_2CF_3$, -CH=CH_2, -$CH_2CH=CH_2$, -CH=$CHCH_3$, cis-$CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(CH_3)$, trans-$CH_2CH=CH(C_6H_5)$, -$CH_2CH=C(CH_3)_2$, cis-$CH_2CH=CHCH_2CH_3$, trans-$CH_2CH=CHCH_2CH_3$, cis-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH_2CH=CH(CH_3)$, trans-$CH_2CH=CHCH_2(C_6H_5)$, -C≡CH, -CH_2C≡CH, -CH_2C≡$C(CH_3)$, -CH_2C≡$C(C_6H_5)$, -CH_2CH_2C≡CH, -CH_2CH_2C≡$C(CH_3)$, -CH_2CH_2C≡$C(C_6H_5)$, -$CH_2CH_2CH_2C$≡CH, -$CH_2CH_2CH_2C$≡$C(CH_3)$, -$CH_2CH_2CH_2C$≡$C(C_6H_5)$, cyclopropyl-CH_2-, cyclobutyl-CH_2-, cyclopentyl-CH_2-, cyclohexyl-CH_2-, (2-CH_3-cyclopropyl)CH_2-, (3-CH_3-cyclobutyl)CH_2-, cyclopropyl-CH_2CH_2-, cyclobutyl-CH_2CH_2-, cyclopentyl-CH_2CH_2-, cyclohexyl-CH_2CH_2-, (2-CH_3-cyclopropyl)CH_2CH_2-, (3-CH_3-cyclobutyl)CH_2CH_2-, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, furanyl-CH_2-, thienyl-CH_2-, pyridyl-CH_2-, 1-imidazolyl-CH_2-, oxazolyl-CH_2-, isoxazolyl-CH_2-, phenyl-CH_2CH_2-, (2-F-phenyl)CH_2CH_2-, (3-F-phenyl)CH_2CH_2-, (4-F-phenyl)CH_2CH_2-, furanyl-CH_2CH_2-, thienyl-CH_2CH_2-, pyridyl-CH_2CH_2-, 1-imidazolyl-CH_2CH_2-, oxazolyl-CH_2CH_2-, or isoxazolyl-CH_2CH_2-;

W is a bond, -CH_2-, or -$CH(CH_3)$-;

X is a bond;





Y is a bond, -CH_2-V-, -V-, or -V-CH_2-;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, -$S(=O)_2$-, -NH-, or -$N(CH_3)$-,

Z is phenyl 2-F-phenyl, 3-F-phenyl, 4-F-phenyl, 2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl, 2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl, 3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl, 2,4-diCl-phenyl, 2,5-diCl-phenyl,

2,6-diCl-phenyl, 3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl, 3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl, 3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl, 4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl, 2-CF_3O-phenyl, 3-CF_3O-phenyl, 4-CF_3O-phenyl, furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl, 4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl, 1-benzimidazolyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino,N-piperinyl, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-, (3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, (2-MeO-phenyl)CH_2-, (3-MeO-phenyl)CH_2-, (4-MeO-phenyl)CH_2-, (2-Me-phenyl)CH_2-, (3-Me-phenyl)CH_2-, (4-Me-phenyl)CH_2-, (2-MeS-phenyl)CH_2-, (3-MeS-phenyl)CH_2-, 4-MeS-phenyl)CH_2-, (2-CF_3O-phenyl)CH_2-, (3-CF_3O-phenyl)CH_2-, (4-CF_3O-phenyl)CH_2-, (furanyl)CH_2-, (thienyl)CH_2-, (pyridyl)CH_2-, (2-Me-pyridyl)CH_2-, (3-Me-pyridyl)CH_2-, (4-Me-pyridyl)CH_2-, (1-imidazolyl)CH_2-, (oxazolyl)CH_2-, (isoxazolyl)CH_2-, (1-benzimidazolyl)CH_2-, (cyclopropyl)CH_2-, (cyclobutyl)CH_2-, (cyclopentyl)CH_2-, (cyclohexyl)CH_2-, (morpholino)CH_2-, (N-pipridinyl)CH_2-, phenyl-CH_2CH_2-, (phenyl)$_2CHCH_2$-, (2-F-phenyl)CH_2CH_2-, (3-F-phenyl)CH_2CH_2-, (4-F-phenyl)CH_2CH_2-, (2-Cl-phenyl)CH_2CH_2-, (3-Cl-phenyl)CH_2CH_2-, (4-Cl-phenyl)CH_2CH_2-, (2,3-diF-phenyl)CH_2CH_2-, (2,4-diF-phenyl)CH_2CH_2-, (2,5-diF-phenyl)CH_2CH_2-, (2,6-diF-phenyl)CH_2CH_2-, (3,4-diF-phenyl)CH_2CH_2-, (3,5-diF-phenyl)CH_2CH_2-, (2,3-diCl-phenyl)CH_2CH_2-, (2,4-diCl-phenyl)CH_2CH_2-, (2,5-diCl-phenyl)CH_2CH_2-, (2,6-diCl-phenyl)CH_2CH_2-, (3,4-diCl-phenyl)CH_2CH_2-, (3,5-diCl-phenyl)CH_2CH_2-, (3-F-4-Cl-phenyl)CH_2CH_2-, (3-F-5-Cl-phenyl)CH_2CH_2-, (3-Cl-4-F-phenyl)CH_2CH_2-, (2-MeO-phenyl)CH_2CH_2-, (3-MeO-phenyl)CH_2CH_2-, (4-MeO-phenyl)CH_2CH_2-, (2-Me-phenyl)CH_2CH_2-, (3-Me-phenyl)CH_2CH_2-, (4-Me-phenyl)CH_2CH_2-, (2-MeS-phenyl)CH_2CH_2-, (3-MeS-phenyl)CH_2CH_2-, (4-MeS-phenyl)CH_2CH_2-, (2-CF_3O-phenyl)CH_2CH_2-, (3-CF_3O-phenyl)CH_2CH_2-, (4-CF_3O-phenyl)CH_2CH_2-, (furanyl)CH_2CH_2-, (thienyl)CH_2CH_2-, (pyridyl)CH_2CH_2-, (2-Me-pyridyl)CH_2CH_2-, (3-Me-pyridyl)CH_2CH_2-,

(4-Me-pyridyl)CH_2CH_2-, (imidazolyl)CH_2CH_2-, (oxazolyl)CH_2CH_2-, (isoxazolyl)CH_2CH_2-, (benzimidazolyl)CH_2CH_2-,(cyclopropyl)CH_2CH_2-, (cyclobutyl)CH_2CH_2-,(cyclopentyl)CH_2CH_2-, (cyclohexyl)CH_2CH_2-, (morpholino)CH_2CH_2-, (N-pipridinyl)CH_2CH_2-, methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl, s-butyl, t-butyl, or allyl;

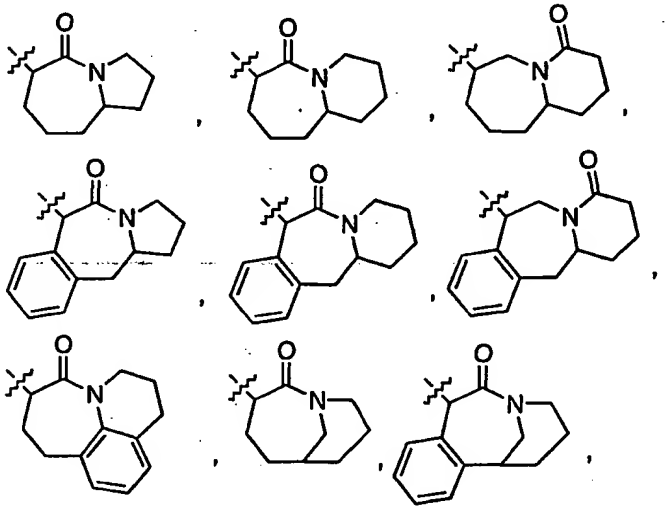
R^{10} is H, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, or (4-CF_3-phenyl)CH_2CH_2-;

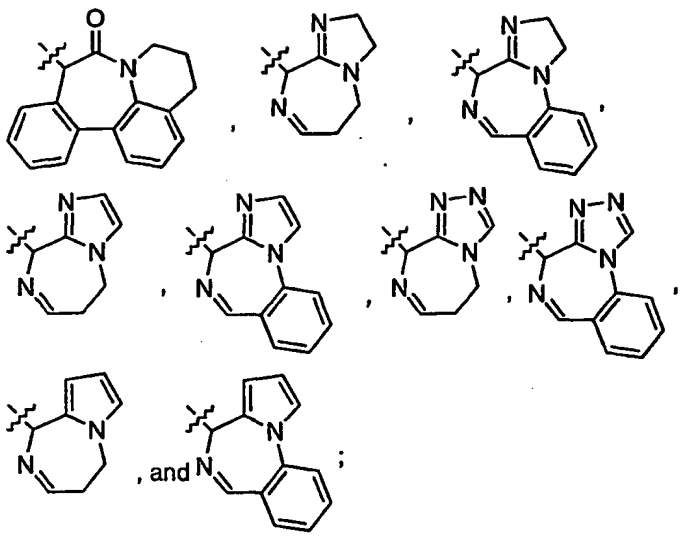
R^{11}, at each occurrence, is independently selected from H, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, or (4-CF_3-phenyl)CH_2CH_2-; and

alternatively, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or a benzo fused radical.

9. A compound of Claim 8 wherein:

ring B, along with up to 2 R^{11}s, is





wherein ring B is further substituted with 0, 1, 2, 3, or 4 R^{11}.

10. A compound of Claim 2 selected from:

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-butyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-methyl-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-(pyrid-2-ylmethyl)-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

(2R, 3S)-3-allyl-2-isobutyl-N^1-(4-(2-(diethylamino)ethyl)-3-oxo-2,3,4,8,9,10-hexahydronaphtho[1,8-ef][1,4]diazepin-2-yl)butanediamide;

N1-(2-benzylcarbamoyl-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-2-isobutyl-3-propyl-succinamide;

N1-[2-(1-benzyl-pyrrolidin-3-ylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide;

N1-[2-(1-benzyl-pyrrolidin-3-ylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide;

2-isobutyl-N1-[2-(4-methoxy-benzylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-3-propyl-succinamide;

2-isobutyl-N1-[2-(3-methoxy-benzylcarbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-3-propyl-succinamide;

N1-[2-(cyclohexylmethyl-carbamoyl)-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl]-2-isobutyl-3-propyl-succinamide;

2-isobutyl-N1-(2-isopropylcarbamoyl-4-oxo-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-3-propyl-succinamide;

2-isobutyl-N1-(4-oxo-2-phenylcarbamoyl-1,2,4,5,6,7-hexahydro-azepino[3,2,1-hi]indol-5-yl)-3-propyl-succinamide;

(2*R*,3*S*)-3-allyl-*N*'-[(7*S*)-2-benzyl-6-oxo-1,2,3,4,6,7,8,10a-octahydropyrazino[1,2-a]azepin-7-yl]-2-isobutylbutanediamide;

N1-(1,5-dioxo-octahydro-pyrrolo[1,2-a][1,4]diazepin-4-yl)-2-isobutyl-3-propyl-succinamide;

N1-(2-benzyloxy-5-oxo-2,3,5,6,7,9a-hexahydro-1H-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide;

N1-(2-benzyloxy-5-oxo-octahydro-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide;

N1-(2-hydroxy-5-oxo-octahydro-pyrrolo[1,2-a]azepin-6-yl)-2-isobutyl-3-propyl-succinamide;

3-allyl-N^1-[3-(4-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(4-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1- [3-(4-benzofuran-2-yl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1- [3-(4-(4-chloro-phenyl)-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(4-(3,5-dimethylisoxazol-4-yl)phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(3-bromo-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide;

3-allyl-N^1-[3-(3-phenyl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide; and

3-allyl-N^1-[3-(3-benzofuran-2-yl-phenyl)-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-a]azepin-9-yl]-2-isobutyl-succinamide.

11. A pharmaceutical composition comprising a compound of one of Claims 1-10 and a pharmaceutically acceptable carrier.

12. A method for the treatment of neurological disorders associated with β amyloid production comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of one of Claims 1-10.

13. A method for the treatment of Alzheimer's Disease associated with β amyloid production comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of one of Claims 1-10.

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(54) Title: SUCCINOYLAMINO CARBOCYCLES AND HETEROCYCLES AS INHIBITORS OF Aβ PROTEIN PRODUCTION

(57) Abstract: This invention relates to novel carbocycles and heterocycles having drug and bio-affecting properties, their pharmaceutical compositions and methods of use. These novel compounds inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurological deposits of amyloid protein. More particularly, the present invention relates to the treatment of neurological disorders related to β-amyloid production such as Alzheimer's disease and Down's Syndrome.

INTERNATIONAL SEARCH REPORT

In' stional Application No
PCT/US 01/05236

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D487/04 C07D471/04 C07D471/08 C07D243/24 A61K31/55
A61K31/551 A61K31/5513 A61K31/5517 A61P25/28
//(C07D487/04,223:00,209:00),(C07D471/04,223:00,221:00),

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99 67221 A (MCDANIEL STACEY L ;AUDIA JAMES E (US); CWI CYNTHIA L (US); ELAN PH) 29 December 1999 (1999-12-29) cited in the application abstract; claims 1-3,14,15,30,58,85-88 ---	1-13
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[X] Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search	Date of mailing of the international search report
12 September 2001	27/09/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hass, C

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/05236

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 (C07D471/08,223:00,221:00),(C07D487/04,241:00,223:00), (C07D487/04,243:00,209:00),(C07D471/04,243:00,221:00), (C07D487/04,243:00,235:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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[X] Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search	Date of mailing of the international search report
12 September 2001	

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hass, C

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International Application No
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